STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 170211

TO: Ben Sackey **Location: rem/5B3/5C18** **Art Unit: 1626** Nov 4, 2005 **Case Serial Number: 10/667087**	**From: P. Sheppard** **Location: Remsen Building** **Phone: (571) 272-2529** **sheppard@uspto.gov**

Search Notes

FOR OFFICIAL USE ONLY

ACCESS DB # 170211

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Paula

Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: DEN SACKETT Examiner #: 73489 Date: 11/1/05

Art Unit: 1626 Phone Number: 2-0704 Serial Number: 10/667,087

Location (Bldg/Room#): REM 5B31 (Mailbox #): REM Results Format Preferred (circle): PAPER DISK

****

5618

MEY

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: 4-Pyrrolidino-phenyl-benzyl ether derivatives

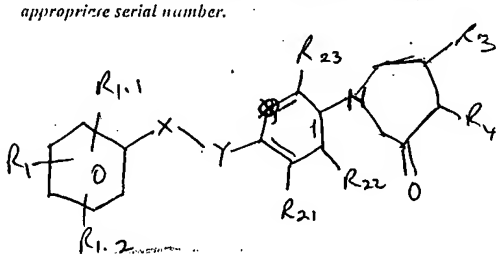
Inventors (please provide full names): Hans Ding et al

Earliest Priority Date: 09/20/02

Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*



Q is =N- or =C(R24)

X and Y -> $-CH_2-CH_2-$, CH=CH or CH_2-O-

R', R1.1 and R1.2 -> H, alkyl, halo, CN etc

****

STAFF USE ONLY

Searcher: _____

Searcher Phone #: _____

Searcher Location: _____

Date Searcher Picked Up: _____

Date Completed: _____

Searcher Prep & Review Time: _____

Online Time: _____

Type of Search

_____ NA Sequence (#)

_____ AA Sequence (#)

_____ Structure (#)

_____ Bibliographic

_____ Litigation

_____ Fulltext

_____ Other

Vendors and cost where applicable

_____ STN _____ Dialog

_____ Questel/Orbit _____ Lexis/Nexis

_____ Westlaw _____ WWW/Internet

____ In-house sequence systems

__Commercial ___Oligomer ____Score/Length

__ Interference ___ SPDI ____ Encode/Transl

_____ Other (specify)

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L5           237 SEA SSS FUL L3
L6              STR
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L14           20 SEA ABB=ON  PLU=ON  ("KRUMMENACHER D"/AU OR "KRUMMENACHER
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L15           45 SEA ABB=ON  PLU=ON  "WIRZ B"/AU OR "WIRZ BEAT"/AU
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L18         1109 SEA ABB=ON  PLU=ON  THOMAS A/AU OR THOMAS A W/AU OR "THOMAS
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L20           13 SEA ABB=ON  PLU=ON  (L12 AND (L13 OR L14 OR L15 OR L16 OR L17
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L25           12 SEA ABB=ON  PLU=ON  L17 AND L18
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                 L25) NOT (L8 OR L11)
                 D STAT QUE NOS
                 D IBIB ABS L26 1-25


     FILE HOME

     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.

     STRUCTURE FILE UPDATES:    3 NOV 2005  HIGHEST RN 866718-46-9
     DICTIONARY FILE UPDATES:   3 NOV 2005  HIGHEST RN 866718-46-9

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

     TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005
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Please note that search-term pricing does apply when conducting SmartSELECT searches.

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**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from  *
* the IDE default display format and the ED field has been added,    *
* effective March 20, 2005.  A new display format, IDERL, is now     *
* available and contains the CA role and document type information.  *
*                                                                    *
**********************************************************************
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Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

FILE HCAPLUS

FILE COVERS 1907 - 4 Nov 2005 VOL 143 ISS 20
FILE LAST UPDATED: 3 Nov 2005 (20051103/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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FILE 'HCAPLUS' ENTERED AT 16:47:19 ON 04 NOV 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 4 Nov 2005  VOL 143 ISS 20
FILE LAST UPDATED: 3 Nov 2005  (20051103/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

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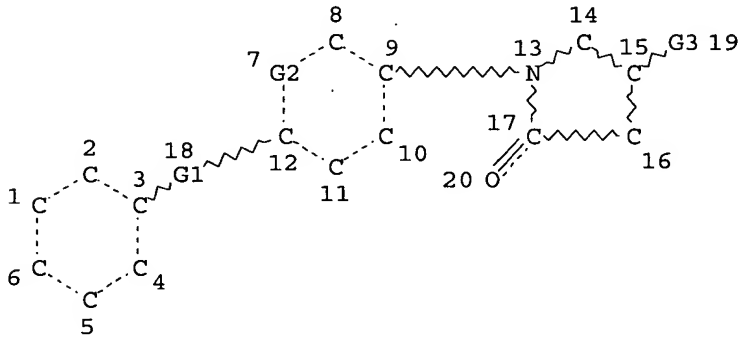


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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS  22

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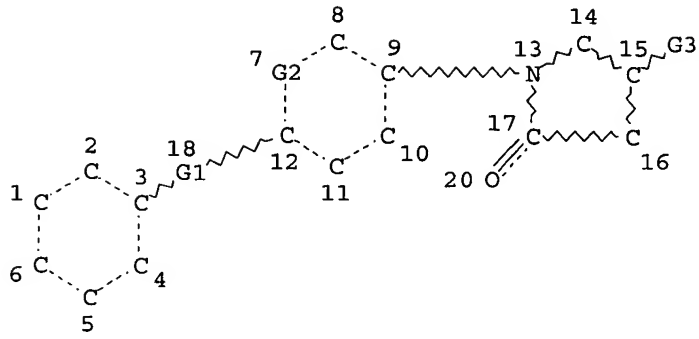

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O≡C~NH2 40 @41 42

O≡C~O~G4 36 @37 38 39

SO2-G4 @43 44

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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 13 9 3
NUMBER OF NODES IS 44

STEREO ATTRIBUTES: NONE
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L8 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L7

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L8 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:259688 HCAPLUS
DOCUMENT NUMBER: 142:315325
TITLE: Chemoenzymic preparation of enantiopure pyrrolidin-2-one derivatives
INVENTOR(S): Iding, Hans; Krummenacher, Daniela; Wirz, Beat; Wostl, Wolfgang
PATENT ASSIGNEE(S): Germany
SOURCE: U.S. Pat. Appl. Publ., 10 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005065204	A1	20050324	US 2004-940155	20040914
WO 2005026373	A1	20050324	WO 2004-EP10290	20040915

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2003-21076 A 20030918

OTHER SOURCE(S): CASREACT 142:315325; MARPAT 142:315325

AB A process is provided for the chemoenzymic preparation of enantiomerically pure (S)-1-(4-hydroxyphenyl)-5-oxo-pyrrolidine-3-carboxylic acid and (R)-1-(4-hydroxyphenyl)-5-oxo-pyrrolidine-3-carboxylic acid esters and their derivs. by kinetic resolution of 1-(4-hydroxyphenyl)-5-oxo-pyrrolidine-3-carboxylic acid esters and derivs. by a cholesterase. The resulting compds. are valuable intermediates that can be used in the synthesis of pharmaceutically active MAOB inhibitors.

IT **676479-39-3P**

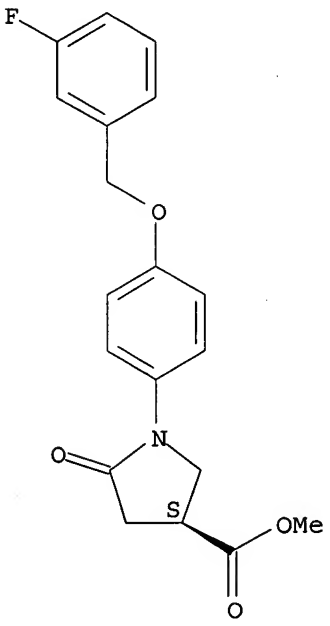
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)

(chemoenzymic preparation of enantiopure pyrrolidin-2-one derivs.)

RN 676479-39-3 HCAPLUS

CN 3-Pyrrolidinecarboxylic acid, 1-[4-[(3-fluorophenyl)methoxy]phenyl]-5-oxo-, methyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **676472-95-0P**

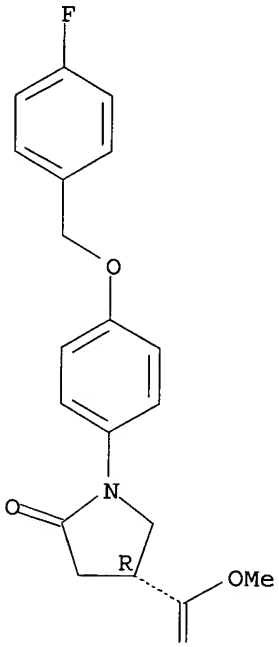
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(chemoenzymic preparation of enantiopure pyrrolidin-2-one derivs.)

RN 676472-95-0 HCAPLUS

CN 3-Pyrrolidinecarboxylic acid, 1-[4-[(4-fluorophenyl)methoxy]phenyl]-5-oxo-, methyl ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

L8 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2004:267296 HCAPLUS
DOCUMENT NUMBER:	140:303520
TITLE:	Preparation of arylpyrrolidones as monoamine oxidase-B (MAO-B) inhibitors
INVENTOR(S):	Iding, Hans; Jolidon, Synese; Krummenacher, Daniela; Rodriguez Sarmiento, Rosa Maria; Thomas, Andrew William; Wirz, Beat; Wostl, Wolfgang; Wyler, Rene
PATENT ASSIGNEE(S):	F. Hoffmann-La Roche A.-G., Switz.
SOURCE:	PCT Int. Appl., 55 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026827	A1	20040401	WO 2003-EP10384	20030918
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2496756	AA	20040401	CA 2003-2496756	20030918
US 2004097578	A1	20040520	US 2003-666594	20030918
US 2004106650	A1	20040603	US 2003-667088	20030918
US 2004116707	A1	20040617	US 2003-667087	20030918
EP 1542969	A1	20050622	EP 2003-748052	20030918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: EP 2002-21319 A 20020920
WO 2003-EP10384 W 20030918

OTHER SOURCE(S): MARPAT 140:303520

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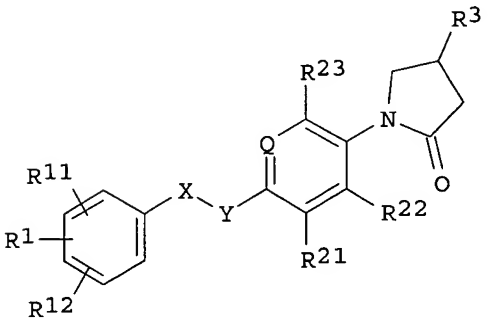

I

AB Title compds. (I; Q = N, CR24; XY = CH2CH2, CH:CH, CH2O; R1, R11, R12 = H, halo, alkyl, haloalkyl, cyano, alkoxy, haloalkoxy; R21, R22, R23 = H, halo; R24 = H, halo, Me; R3 = CONHMe, CH2CN), were prepared Thus, Me 1-(4-hydroxyphenyl)-5-oxopyrrolidine-3-carboxylate (preparation given), K2CO3, and 3-fluorobenzyl bromide were refluxed 5 h in EtCOMe to give 24% Me 1-[4-(3-fluorobenzyloxy)phenyl]-5-oxopyrrolidine-3-carboxylate. The latter was heated with MeNH2 in EtOH/DMF in a sealed vessel at 120° for 48 h to give 31% 1-[4-(3-fluorobenzyloxy)phenyl]-5-oxopyrrolidine-3-carboxylic acid methylamide. Preferred I inhibited MAO-B with IC50 ≤1μM.

IT **676473-25-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of arylpyrrolidones as monoamine oxidase-B inhibitors)

RN 676473-25-9 HCAPLUS

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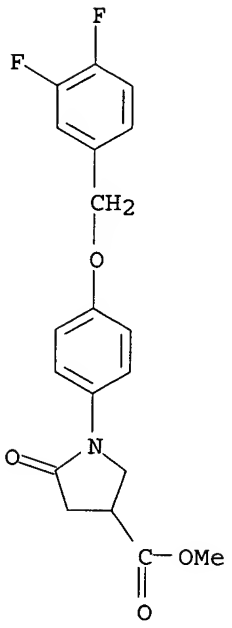

IT **133748-39-7P**, 1-(4-Benzyloxyphenyl)-5-oxopyrrolidine-3-carboxylic acid methyl ester **676472-76-7P**, 1-[4-(3-Fluorobenzyloxy)phenyl]-5-oxopyrrolidine-3-carboxylic acid methyl ester **676472-77-8P**, 1-[4-(4-Fluorobenzyloxy)phenyl]-5-oxopyrrolidine-3-carboxylic acid methyl ester **676472-80-3P**, 1-[4-(3-Fluorobenzyloxy)-3-methylphenyl]-5-oxopyrrolidine-3-carboxylic acid methyl ester **676472-95-0P**, (R)-1-[4-(4-Fluorobenzyloxy)phenyl]-5-oxopyrrolidine-3-carboxylic acid methyl ester **676472-97-2P**, (R)-1-[4-(3-Fluorobenzyloxy)phenyl]-5-oxopyrrolidine-3-carboxylic acid methyl ester **676472-98-3P**, (R)-1-[4-(3-Chlorobenzyloxy)phenyl]-5-oxopyrrolidine-3-carboxylic acid methyl ester **676473-00-0P**, (R)-1-[4-(2,6-Difluorobenzyloxy)phenyl]-5-oxopyrrolidine-3-carboxylic acid methyl ester **676473-02-2P**, (R)-1-[4-(2,4,6-Trifluorobenzyloxy)phenyl]-5-oxopyrrolidine-3-carboxylic acid methyl ester **676473-09-9P** **676473-12-4P** **676473-15-7P** **676473-17-9P** **676473-20-4P** **676473-22-6P** **676473-24-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of arylpyrrolidones as monoamine oxidase-B inhibitors)

RN 133748-39-7 HCAPLUS

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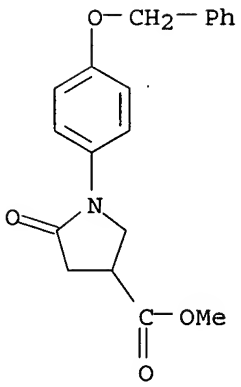

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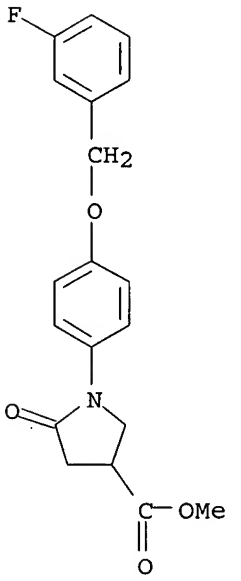

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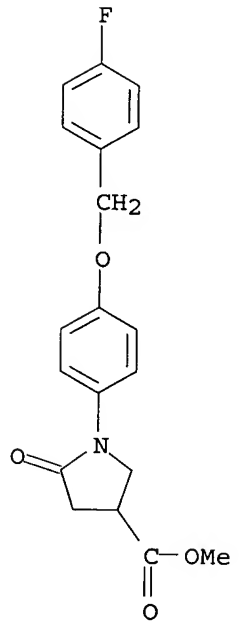

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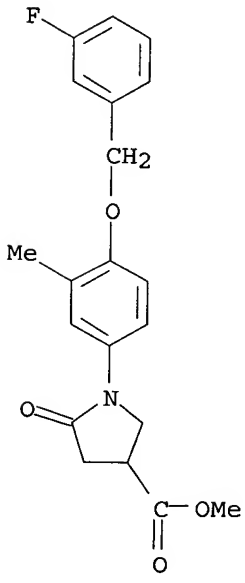
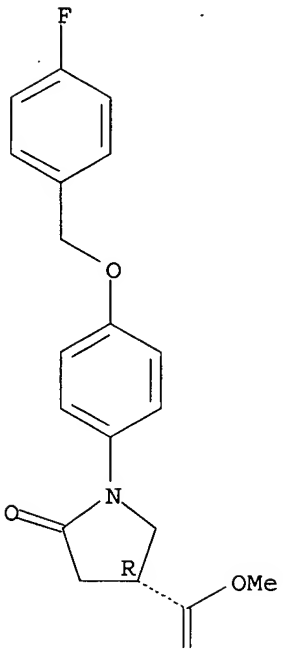


RN 676472-95-0 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[4-[(4-fluorophenyl)methoxy]phenyl]-5-oxo-, methyl ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

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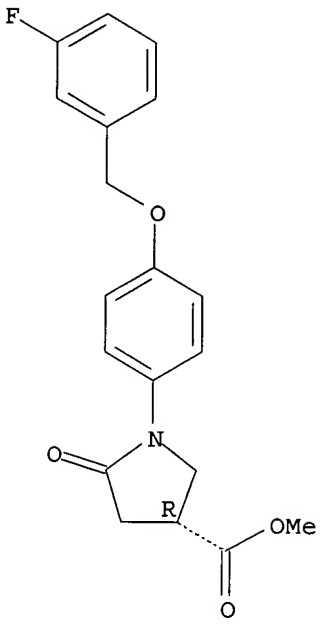
Absolute stereochemistry.



RN 676472-98-3 HCAPLUS
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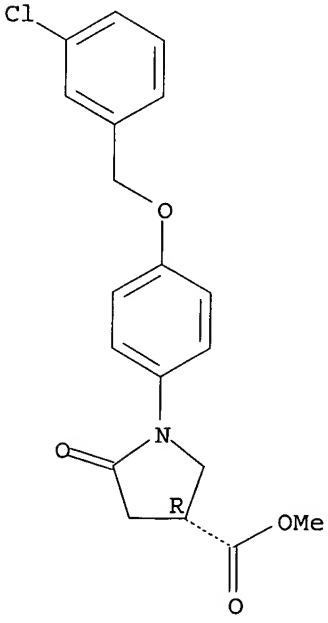
Absolute stereochemistry.



RN 676473-00-0 HCAPLUS
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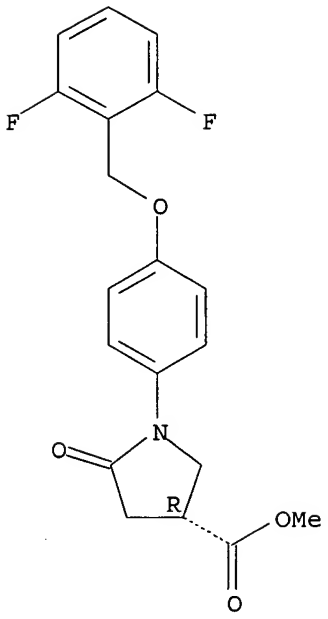
Absolute stereochemistry.



RN 676473-02-2 HCAPLUS
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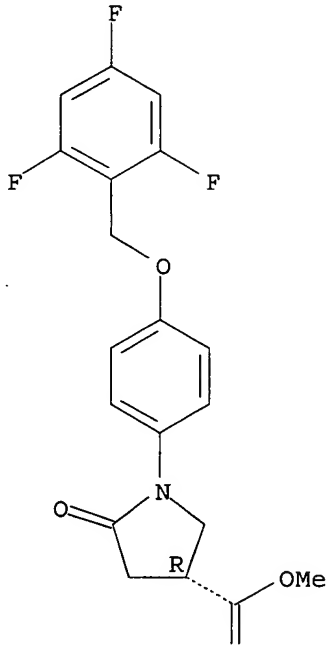
Absolute stereochemistry.

PAGE 1-A



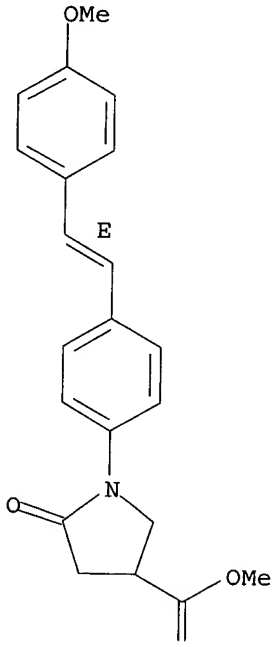
PAGE 2-A

O

RN 676473-09-9 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[4-[(1E)-2-(4-methoxyphenyl)ethenyl]phenyl]-5-oxo-, methyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A

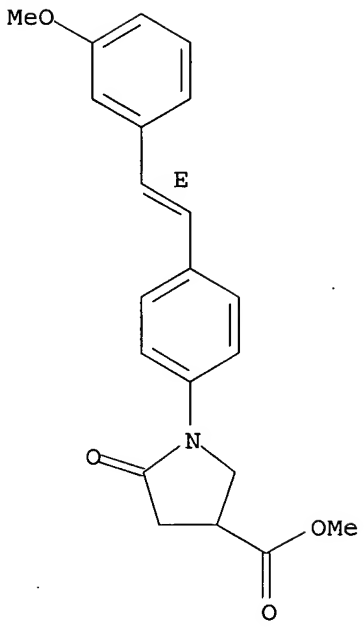


PAGE 2-A

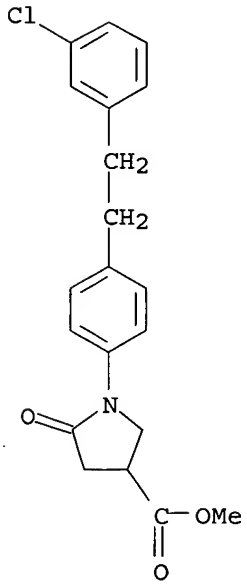
O

RN 676473-12-4 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[4-[(1E)-2-(3-methoxyphenyl)ethenyl]phenyl]-5-oxo-, methyl ester (9CI) (CA INDEX NAME)

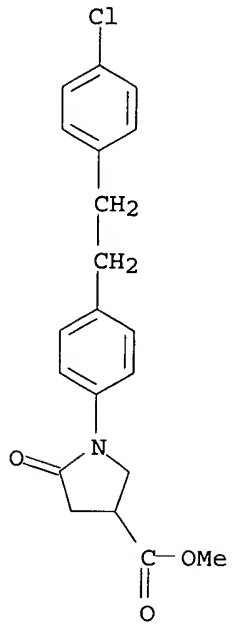
Double bond geometry as shown.



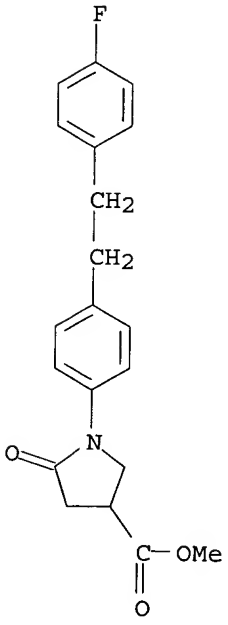
RN 676473-15-7 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[4-[2-(3-chlorophenyl)ethyl]phenyl]-5-oxo-, methyl ester (9CI) (CA INDEX NAME)



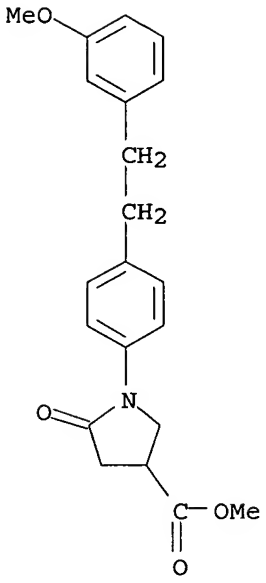
RN 676473-17-9 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[4-[2-(4-chlorophenyl)ethyl]phenyl]-5-oxo-, methyl ester (9CI) (CA INDEX NAME)



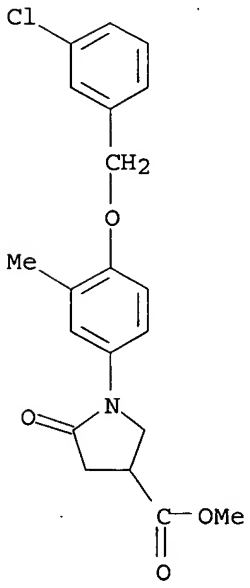
RN 676473-20-4 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[4-[2-(4-fluorophenyl)ethyl]phenyl]-5-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 676473-22-6 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[4-[2-(3-methoxyphenyl)ethyl]phenyl]-5-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 676473-24-8 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[4-[(3-chlorophenyl)methoxy]-3-methylphenyl]-5-oxo-, methyl ester (9CI) (CA INDEX NAME)



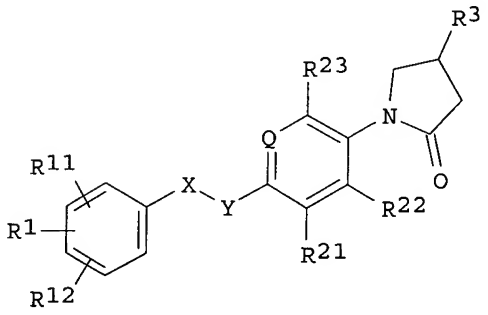
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:267294 HCAPLUS
DOCUMENT NUMBER: 140:303519
TITLE: Preparation of arylpyrrolidones as monoamine oxidase-B (MAO-B) inhibitors.

INVENTOR(S): Iding, Hans; Jolidon, Synese; Krummenacher, Daniela; Rodriguez-Sarmiento, Rosa Maria; Thomas, Andrew William; Wirz, Beat; Wostl, Wolfgang; Wyler, Rene
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026825	A1	20040401	WO 2003-EP10356	20030918
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2498785	AA	20040401	CA 2003-2498785	20030918
US 2004097578	A1	20040520	US 2003-666594	20030918
US 2004106650	A1	20040603	US 2003-667088	20030918
US 2004116707	A1	20040617	US 2003-667087	20030918
EP 1542970	A1	20050622	EP 2003-750564	20030918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003014631	A	20050802	BR 2003-14631	20030918
PRIORITY APPLN. INFO.:			EP 2002-21319 A	20020920
			WO 2003-EP10356 W	20030918

OTHER SOURCE(S): MARPAT 140:303519
GI



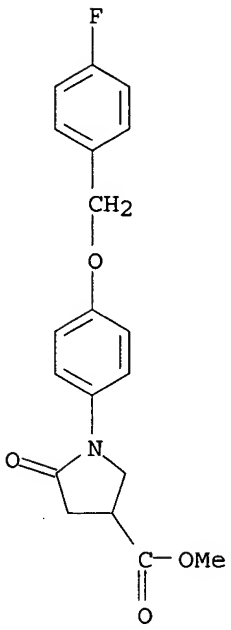
I

AB Title compds. (I; Q = N, CR24; XY = CH2CH2, CH:CH, CH2O; R1, R11, R12 = H, halo, haloalkyl, cyano, alkoxy, haloalkoxy; R21, R22, R23 = H, halo; R24 = H, halo, Me; R3 = NHR6; R6 = CHO, alkylcarbonyl, haloalkylcarbonyl, alkoxycarbonyl, CONH2, alkylsulfonyl), were prepared Thus, a mixture of 4-benzyloxyaniline and itaconic acid was heated at 130° for 20 min. to give 96% 1-(4-benzyloxyphenyl)-5-oxopyrrolidine-3-carboxylic acid, which was converted to N-[1-[4-(3-fluorobenzyloxy)phenyl]-5-oxopyrrolidin-3-yl]acetamide in several steps. Preferred I inhibited MAO-B with IC50

≤1 μM.

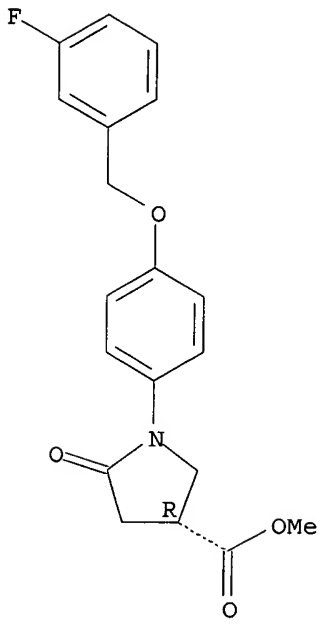
IT **676472-77-8P 676472-97-2P 676479-39-3P 676479-46-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of arylpyrrolidones as monoamine oxidase-B (MAO-B) inhibitors)

RN 676472-77-8 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[4-[(4-fluorophenyl)methoxy]phenyl]-5-oxo-, methyl ester (9CI) (CA INDEX NAME)



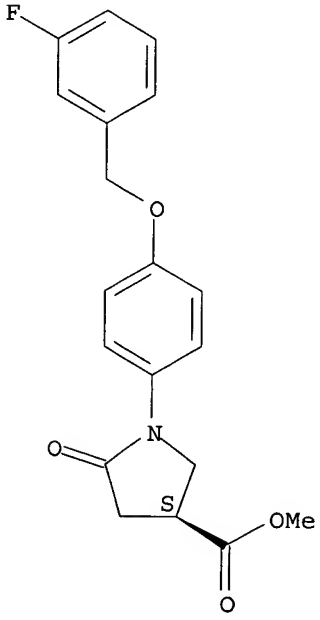
RN 676472-97-2 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[4-[(3-fluorophenyl)methoxy]phenyl]-5-oxo-, methyl ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

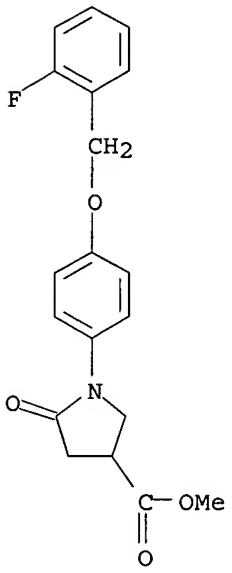


RN 676479-39-3 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[4-[(3-fluorophenyl)methoxy]phenyl]-5-oxo-, methyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

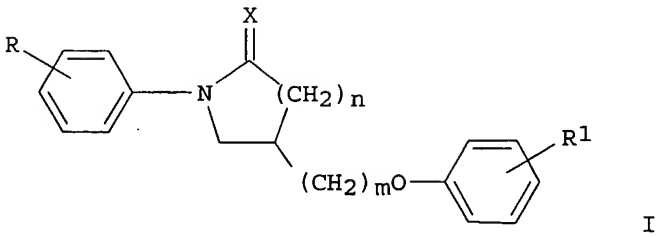


RN 676479-46-2 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[4-[(2-fluorophenyl)methoxy]phenyl]-5-oxo-, methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:239257 HCAPLUS
DOCUMENT NUMBER: 122:105605
TITLE: Synthesis of 4-[1-(substituted phenyl)-2-oxo-pyrrolidin-4-yl]methyloxybenzoic acids and related compounds, and their inhibitory capacities toward fatty-acid and sterol biosynthesis
AUTHOR(S): Watanabe, S.; Ogawa, K.; Ohno, T.; Yano, S.; Yamada, H.; Shirasaka, T.
CORPORATE SOURCE: Fujii Mem. Res. Lab., Otsuka Pharmaceutical Co. Ltd., Otsu, Shiga, 520-01, Japan
SOURCE: European Journal of Medicinal Chemistry (1994), 29(9), 675-86
CODEN: EJMCA5; ISSN: 0223-5234
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

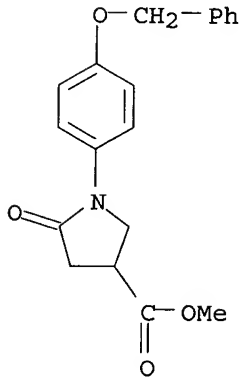
AB The synthesis of a series of 4-[1-(substituted phenyl)-2-oxo-pyrrolidin-4-yl]methyloxybenzoic acids and related compds., I (R = H, 4-F, 3-Cl, 4-HO, 3,4-Cl2, etc., R1 = 2-, 3-, 4-CO2H, 4-CH:CHCO2H, 4-CH2CH2CO2H, X = O, H2, m = 1, 2, n = 1, 2) and their evaluation for inhibitory capacity toward

fatty-acid and sterol biosyntheses using rats' liver slices in vitro and rabbits in vivo, are described. Several compds. showed a potent inhibitory activity toward fatty-acid and sterol biosyntheses. Their IC50s were 4.4-6.8 + 10-6 M and 6.6-9.8 + 10-6 M. These activities were always superior to those of Clinofibrate as reference The inhibitory activity toward the sterol biosynthesis of these compds. was inferior to that of Pravastatin. The reducing effects of two representative compds. I (R = 4-Cl, 4-CMe3, R1 = 4-CO2H, X = O, m = 1, n = 1) (II) toward plasma cholesterols and triglyceride were evaluated in Japanese white rabbits (30 and 100 mg/kg, po) and compared with those of Clinofibrate and Pravastatin. The compds. showed a similar hypocholesterolemic effect to Pravastatin and a more potent hypotriglycermic effect than Clinofibrate and Pravastatin in this animal model. Thus, a dual action of hypolipidemic effects was noted in II compared with the reference

IT **133748-39-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (oxopyrrolidinyl)methyloxybenzoic acid derivs. and inhibition of fatty acid and sterol biosynthesis)

RN 133748-39-7 HCAPLUS

CN 3-Pyrrolidinecarboxylic acid, 5-oxo-1-[4-(phenylmethoxy)phenyl]-, methyl ester (9CI) (CA INDEX NAME)



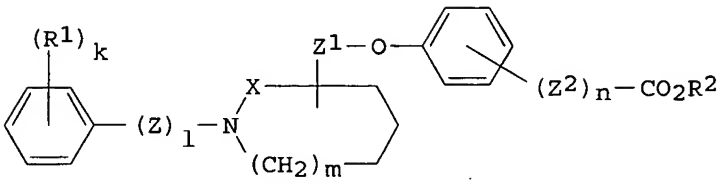
L8 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:228741 HCAPLUS
DOCUMENT NUMBER: 114:228741
TITLE: Preparation of 4-[1-(substituted)phenyl-2-pyrrolidon-4-yl]methoxybenzoic acids and analogs as hypolipidemics
INVENTOR(S): Fujii, Setsuro; Kawamura, Hiroyuki; Watanabe, Shinichi
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 41 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 393607	A2	19901024	EP 1990-107302	19900418
EP 393607	A3	19920122		

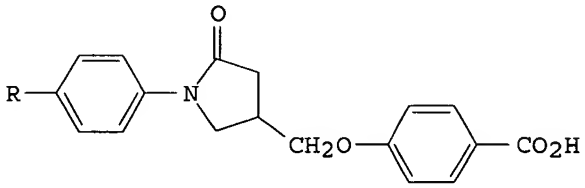
EP 393607	B1	19960221			
R: CH, DE, DK, ES, FR, GB, IT, LI, NL, SE					
JP 03275666	A2	19911206	JP 1990-103834		19900418
ES 2087097	T3	19960716	ES 1990-107302		19900418
KR 156741	B1	19981116	KR 1990-5401		19900418
US 5145865	A	19920908	US 1990-511344		19900419
PRIORITY APPLN. INFO.:			JP 1989-101439	A	19890419
			JP 1990-30839	A	19900209

OTHER SOURCE(S): MARPAT 114:228741

GI



I



II

AB The title compds. [I; R1 = HO, halo, (un)substituted C1-6 alkyl, (un)substituted C3-8 cycloalkyl, (un)substituted PhO, carboxyl, amino, C2-6 alkenyloxy, C1-6 alkylsulfonyloxy, etc.; (R1)k = C1-4 alkylenedioxy, R2 = H, C1-6 alkyl; X = CH2, CO; Z = C1-6 alkylene, alkylenoxy; Z1 = C1-6 alkylene; Z2 = C1-6 alkylene, C2-6 alkenylene; k = 0-3; l, m, n = 0, 1] and their salts, effective hypolipidemics useful for the prophylaxis and treatment of arteriosclerosis, obesity, and diabetes, were prepared Cyclocondensation of p-toluidine with itaconic acid gave Me 1-(4-tolyl)-5-oxo-3-pyridinecarboxylate. This was esterified by MeOH and the ester underwent successive reduction by NaBH4, esterification of the resulting hydroxymethyl derivative by MeSO2Cl, etherification of the mesylate ester by Me p-hydroxybenzoate, saponification, and neutralization by HCl to give title compound II (R = Me). II (R = F) in vitro inhibited biosynthesis of sterol with IC50 of 6.6-28.43 μM and that of fatty acids with IC50 of 5.2-18.44 μM.

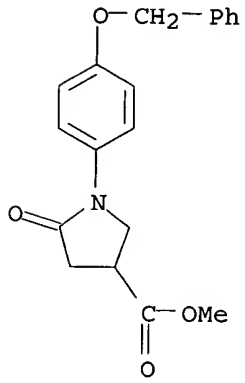
IT **133748-39-7P 133748-41-1P 133748-44-4P 133748-47-7P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

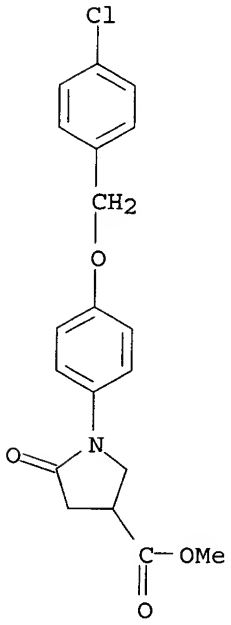
(preparation and reaction of, in preparation of hypolipidemic)

RN 133748-39-7 HCAPLUS

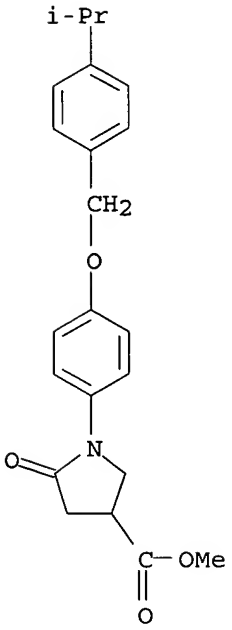
CN 3-Pyrrolidinecarboxylic acid, 5-oxo-1-[4-(phenylmethoxy)phenyl]-, methyl ester (9CI) (CA INDEX NAME)



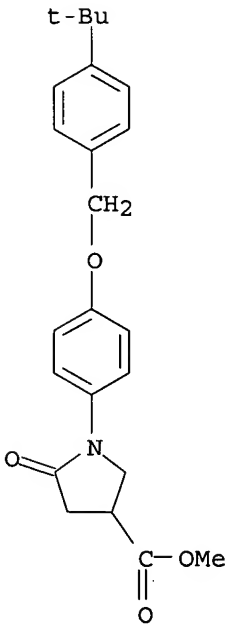
RN 133748-41-1 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[4-[(4-chlorophenyl)methoxy]phenyl]-5-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 133748-44-4 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[4-[[4-(1-methylethyl)phenyl]methoxy]phenyl]-5-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 133748-47-7 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[4-[[4-(1,1-dimethylethyl)phenyl]methoxy]phenyl]-5-oxo-, methyl ester (9CI) (CA INDEX NAME)



L8 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1984:174812 HCAPLUS
DOCUMENT NUMBER: 100:174812
TITLE: N-Aryloxazolidinones and pyrrolidinones
INVENTOR(S): Ancher, Jean Francois; Bourgery, Guy; Douzon, Colette;

Dostert, Philippe; Guerret, Patrick; Lacour, Alain; Langlois, Michel

PATENT ASSIGNEE(S): Delalande S. A. , Fr.
SOURCE: Patentschrift (Switz.), 5 pp.
CODEN: SWXXAS

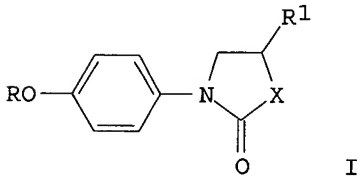
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CH 639962	A	19831215	CH 1980-2161	19800319
FR 2428032	A1	19800104	FR 1978-17388	19780609
FR 2428032	B1	19811016		
FR 2435473	A2	19800404	FR 1978-24024	19780817
FR 2435473	B2	19820122		
ZA 7902799	A	19800827	ZA 1979-2799	19790606
AU 7947862	A1	19791213	AU 1979-47862	19790607
AU 525787	B2	19821202		
CH 642069	A	19840330	CH 1979-5400	19790608
US 4287351	A	19810901	US 1980-119073	19800206
ES 490111	A1	19801216	ES 1980-490111	19800331
AU 525942	B2	19821209	AU 1980-57880	19800429
AU 8057880	A1	19800717		
US 4413001	A	19831101	US 1982-388867	19820616
US 4435415	A	19840306	US 1982-389136	19820616
US 4526786	A	19850702	US 1982-388866	19820616

PRIORITY APPLN. INFO.:

FR 1978-17388	A	19780609
FR 1978-24024	A	19780817
CH 1979-5400	A	19790608
US 1979-45143	A	19790604
ES 1979-481909	A1	19790608

GI



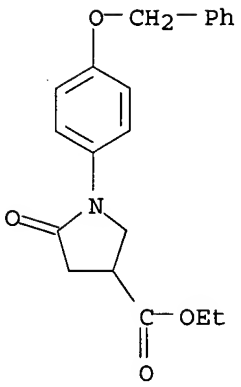
I

AB Psychotropic (no data) title compds. I (X = O, CH2; R = H, CH2Ph; R1 = CH2OR2, CO2Et, CO2H; R2 = H, alkyl) were prepared Thus 4-PhCH2OC6H4NHCH2CH(OH)CH2OH was treated with (EtO)2CO to give I (X = O, R = CH2Ph, R1 = CH2OH) which was hydrogenolyzed to give 73% I (X = O, R = H, R1 = CH2OH).

IT **73422-91-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reduction of)

RN 73422-91-0 HCAPLUS

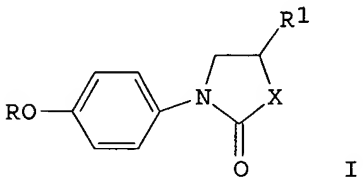
CN 3-Pyrrolidinecarboxylic acid, 5-oxo-1-[4-(phenylmethoxy)phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



L8 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1983:72081 HCAPLUS
DOCUMENT NUMBER: 98:72081
TITLE: N-Aryloxazolidinones and -pyrrolidinones
INVENTOR(S): Ancher, Jean Francois; Bourgery, Guy; Dostert, Philippe; Douzon, Colette; Guerret, Patrick; Lacour, Alain; Langlois, Michel
PATENT ASSIGNEE(S): Delalande S. A. , Fr.
SOURCE: Fr. Demande, 20 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2500831	A1	19820903	FR 1981-3954	19810227
FR 2500831	B1	19840224		
PRIORITY APPLN. INFO.:			FR 1981-3954	19810227

OTHER SOURCE(S): CASREACT 98:72081
GI

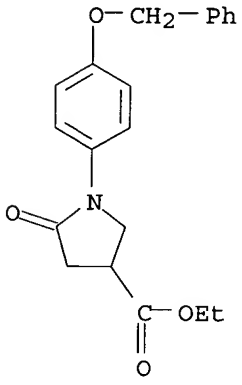


I

AB The title compds. I (X = O, CH2; R = H, CH2Ph; R1 = alkoxymethyl, CH2OH, CO2H, CO2Et) were prepared Thus, Me2CHOCH2CH(OH)CH2Cl was treated with 4-PhCH2OC6H4NH2 and ClCOCl to give 4-PhCH2OC6H4NHCO2CH(CH2Cl)CH2OCHMe2 which was cyclized to I (X = O, R = CH2Ph, R1 = CH2OCHMe2 II). II had ED50 in the reserpine ptosis test of 8.8 mg/kg orally in mice.

IT **73422-91-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reduction of)

RN 73422-91-0 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 5-oxo-1-[4-(phenylmethoxy)phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



L8 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1981:532868 HCAPLUS
DOCUMENT NUMBER: 95:132868
TITLE: N-Aryl azolones and their use in therapy
INVENTOR(S): Ancher, Jean Francois; Bourgery, Guy; Dostert, Philippe; Douzon, Colette; Guerret, Patrick; Lacour, Alain; Langlois, Michel
PATENT ASSIGNEE(S): Delalande S. A., Fr.
SOURCE: Fr. Demande, 83 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2458547	A2	19810102	FR 1980-12423	19800604
FR 2458547	B2	19860516		
US 4348393	A	19820907	US 1979-45143	19790604
US 4287351	A	19810901	US 1980-119073	19800206
ES 490111	A1	19801216	ES 1980-490111	19800331
CA 1171865	A1	19840731	CA 1981-377905	19810520
GB 2076813	A	19811209	GB 1981-15597	19810521
GB 2076813	B2	19840830		
CH 650780	A	19850815	CH 1981-3393	19810525
SE 8103307	A	19811205	SE 1981-3307	19810526
SE 457259	B	19881212		
SE 457259	C	19890413		
ES 502546	A1	19820401	ES 1981-502546	19810527
ZA 8103567	A	19820630	ZA 1981-3567	19810527
AU 8171319	A1	19811210	AU 1981-71319	19810603
AU 544542	B2	19850606		
BE 889091	A4	19811204	BE 1981-204995	19810604
NL 8102715	A	19820104	NL 1981-2715	19810604
JP 57053473	A2	19820330	JP 1981-86312	19810604
JP 02037354	B4	19900823		
DE 3122291	A1	19820513	DE 1981-3122291	19810604

US 4413001	A	19831101	US 1982-388867	19820616
US 4435415	A	19840306	US 1982-389136	19820616
US 4526786	A	19850702	US 1982-388866	19820616
US 4517197	A	19850514	US 1983-518320	19830729
JP 03197470	A2	19910828	JP 1990-13793	19900125
JP 04004311	B4	19920127		

PRIORITY APPLN. INFO.:

US 1979-45143	A	19790604
FR 1978-17388	A	19780609
FR 1978-24024	A	19780817
BE 1979-195621		19790607
BE 1979-876831	A	19790607
ES 1979-481909	A1	19790608
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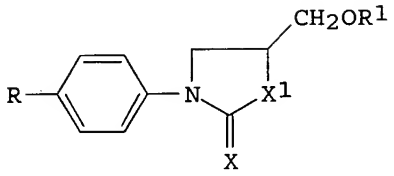

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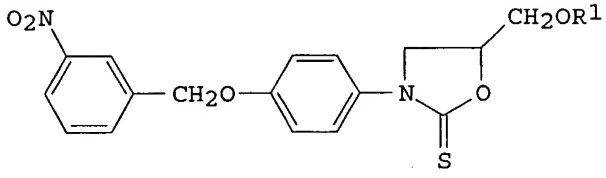


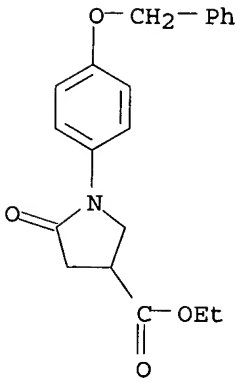
II

AB Azolones I (X = O, S, H2; X1 = O, S, CH2; R = optionally substituted Ph, NH2, CH:CHPh, C.tplbond.CPh, alkyl, alkoxy; R1 = H, alkyl, acyl) were prepared Thus II (R1 = EtCO) was obtained in 73% yield by esterifying II (R1 = H). II (R1 = EtCO) had a ED50 of 4.2 mg/kg orally in mice in the reserpine antagonism test.

IT **73422-91-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reduction of)

RN 73422-91-0 HCAPLUS

CN 3-Pyrrolidinecarboxylic acid, 5-oxo-1-[4-(phenylmethoxy)phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



L8 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1980:426429 HCAPLUS
DOCUMENT NUMBER: 93:26429
TITLE: N-Aryloxazolidinones, -oxazolidinethiones, pyrrolidinones, -pyrrolidines, and thiazolidinones
INVENTOR(S): Douzon, Colette; Ancher, Jean Francois; Bourgery, Guy; Dostert, Philippe; Cuerret, Patrick; Lacour, Alain; Langlois, Michel
PATENT ASSIGNEE(S): Delalande S. A., Fr.
SOURCE: Ger. Offen., 100 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2923295	A1	19791213	DE 1979-2923295	19790608
DE 2923295	C2	19871223		
FR 2428032	A1	19800104	FR 1978-17388	19780609
FR 2428032	B1	19811016		
FR 2435473	A2	19800404	FR 1978-24024	19780817
FR 2435473	B2	19820122		
ZA 7902799	A	19800827	ZA 1979-2799	19790606
CA 1129859	A1	19820817	CA 1979-329220	19790606
BE 876831	A1	19791207	BE 1979-195621	19790607
SE 7904970	A	19791210	SE 1979-4970	19790607
SE 446733	B	19861006		
SE 446733	C	19870122		
AU 7947862	A1	19791213	AU 1979-47862	19790607
AU 525787	B2	19821202		
NL 7904528	A	19791211	NL 1979-4528	19790608
GB 2028306	A	19800305	GB 1979-20102	19790608
GB 2028306	B2	19830112		
ES 481909	A1	19801101	ES 1979-481909	19790608
GB 2054575	A	19810218	GB 1980-21771	19790608
GB 2054575	B2	19821110		
JP 55051064	A2	19800414	JP 1979-72954	19790609
JP 63005391	B4	19880203		
US 4287351	A	19810901	US 1980-119073	19800206
SE 8001674	A	19800304	SE 1980-1674	19800304

SE 447381	B	19861110			
SE 447381	C	19870219			
NL 8001539	A	19800630	NL 1980-1539		19800314
ES 490111	A1	19801216	ES 1980-490111		19800331
ES 490113	A1	19801216	ES 1980-490113		19800331
ES 490114	A1	19801216	ES 1980-490114		19800331
ES 490112	A1	19810116	ES 1980-490112		19800331
ES 490110	A1	19810901	ES 1980-490110		19800331
AU 525942	B2	19821209	AU 1980-57880		19800429
AU 8057880	A1	19800717			
JP 56167666	A2	19811223	JP 1981-67722		19810507
JP 03009106	B4	19910207			
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US 4435415	A	19840306	US 1982-389136		19820616
US 4526786	A	19850702	US 1982-388866		19820616
PRIORITY APPLN. INFO.:			FR 1978-17388	A	19780609
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			ES 1979-481909	A1	19790608

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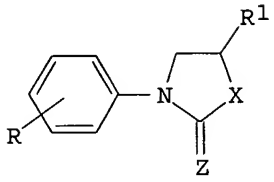

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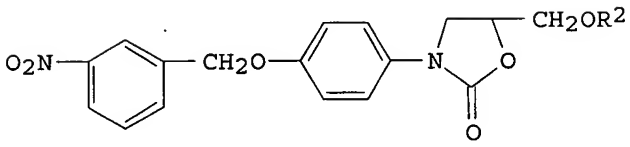


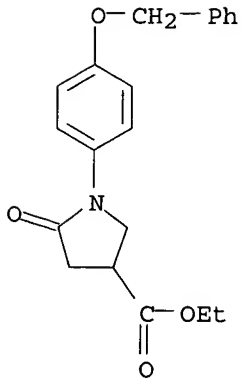
II

AB The title heterocycles I [R = (substituted) alkoxy, cycloalkylalkoxy, acylalkoxy; R1 = esterified or etherified CH2OH, NMe2, (substituted) aminomethyl; X = O, CH2, S; Z = O, H2, S], useful as antidepressants (extensive data tabulated), were prepared by many methods. Thus, acetylating oxazolidinone II (R2 = H) with AcCl and NEt3 in CHCl3 12 h at room temperature gave 72% II (R2 = Ac).

IT **73422-91-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reduction of)

RN 73422-91-0 HCAPLUS

CN 3-Pyrrolidinecarboxylic acid, 5-oxo-1-[4-(phenylmethoxy)phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



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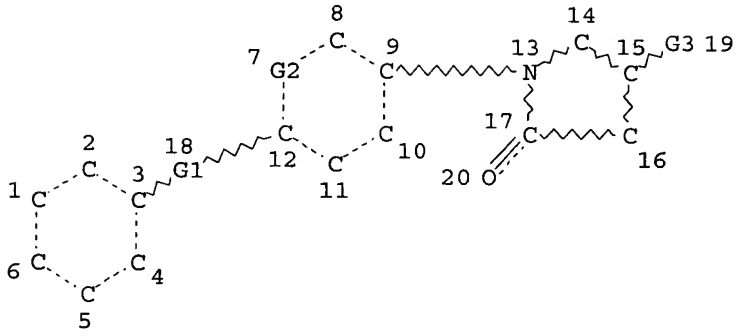

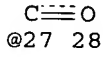

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DEFAULT ECLEVEL IS LIMITED

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NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
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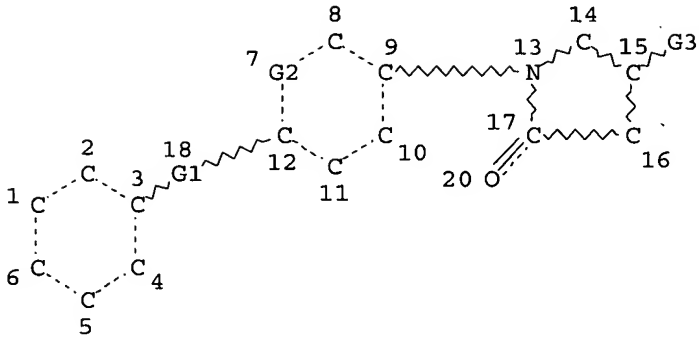

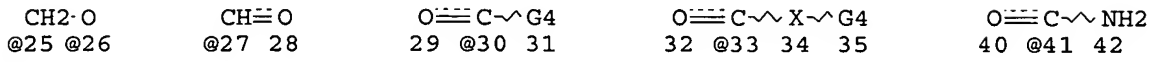

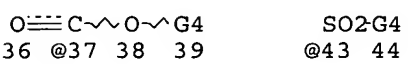

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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 13 9 3
NUMBER OF NODES IS 44

STEREO ATTRIBUTES: NONE

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L11  ANSWER 1 OF 5  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2004:696342  HCAPLUS
DOCUMENT NUMBER:          141:225302
TITLE:                    Preparation of N-arylheterocycles as melanin
                          concentrating hormone (MCH) antagonists.
INVENTOR(S):              Schwink, Lothar; Stengelin, Siegfried; Gossel,
                          Matthias; Boehme, Thomas; Hessler, Gerhard; Stahl,
                          Petra; Gretzke, Dirk
PATENT ASSIGNEE(S):       Aventis Pharma Deutschland GmbH, Germany
SOURCE:                   PCT Int. Appl., 390 pp.
                          CODEN: PIXXD2
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DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004072025	A2	20040826	WO 2004-EP1342	20040213
WO 2004072025	A3	20041223		

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10306250	A1	20040909	DE 2003-10306250		20030214
CA 2516118	AA	20040826	CA 2004-2516118		20040213
US 2004220191	A1	20041104	US 2004-779853		20040217
PRIORITY APPLN. INFO.:			DE 2003-10306250	A	20030214
			US 2003-488545P	P	20030718
			WO 2004-EP1342	W	20040213

OTHER SOURCE(S): MARPAT 141:225302
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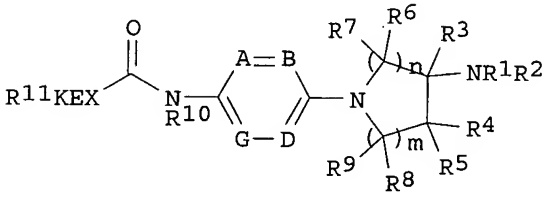


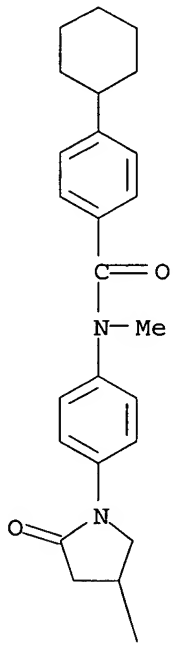
I

AB Title compds. [I; R1, R2 = H, alkyl, alkoxyalkyl, aryloxyalkyl, alkylcarbonyl, alkenylcarbonyl, etc.; R1R2N = atoms to form a 4-10 membered mono-, bi-, or spirocyclic (substituted) ring; R3 = H, alkyl; R4, R5 = H, alkyl, OH, alkoxy, alkylcarbonyloxy, alkylthio; R6-R9 = H, alkyl; R6R7, R8R9 = O; A, B, D, G = N, CR42; AB, DG = CR42; R42 = H, F, Cl, Br, iodo, CF3, NO2, cyano, OCF3, alkoxy, alkylthio, alkenyl, cycloalkyl, cycloalkoxy, cycloalkenyl, alkynyl, CO2H, etc.; R10 = H, alkyl, alkenyl, alkynyl; X = NR52, O, bond, C:C, C.tplbond.C, etc.; R52 = H, alkyl; E = (substituted) C3-14 carbocyclyl, heterocyclyl; K = bond, O, CH2O, S, SO, CO, C:C, C.tplbond.C, etc.; R11 = H, alkyl, alkoxyalkyl, alkenyl, alkynyl, 3-10 membered (substituted) mono-, bi-, tri- or spirocyclic ring; EKR11 = (unsatd.) tricyclic ring; m, n = 0-2], were prepared Thus, N-[1-(4-aminophenyl)pyrrolidin-3-yl]piperidine was treated with carbonyldiimidazole and then with 4-(4-chlorophenyl)piperidine to give 4-(4-chlorophenyl)piperidine-1-carboxylic acid [4-[3-(acetylmethylamino)pyrrolidin-1-yl]phenyl]amide. The latter at 30 mg/kg orally in female NMRI mice reduced milk consumption by 64%.

IT **748183-77-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(preparation of N-arylheterocycles as MCH antagonists)
RN 748183-77-9 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[4-[(4-cyclohexylbenzoyl)methylamino]phenyl]-5-oxo- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

L11 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1976:106114 HCAPLUS
DOCUMENT NUMBER: 84:106114
TITLE: Synthesis of polysulfone-imides
AUTHOR(S): Matsuda, Itsuo; Akiyama, Keiichi; Mizuta, Masateru
CORPORATE SOURCE: Toshiba Res. Dev. Cent., Toshiba Chem. Co., Ltd., Kawasaki, Japan
SOURCE: Kobunshi Ronbunshu (1976), 33(1), 47-51
CODEN: KBRBA3; ISSN: 0386-2186
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
GI For diagram(s), see printed CA Issue.
AB The title polymers were prepared by solution polymerization of O(C6H4SO2H-p)2 and I [R
= p-C6H4CH2C6H4-p, p-C6H4OC6H4-p, m-C6H4(NHCOC6H4-p)2, m-C6H4, (CH2)6] in AcNMe2. Catalytic effect by small amount of water [7732-18-5] was observed The structures of the polymers obtained were determined by comparing their IR

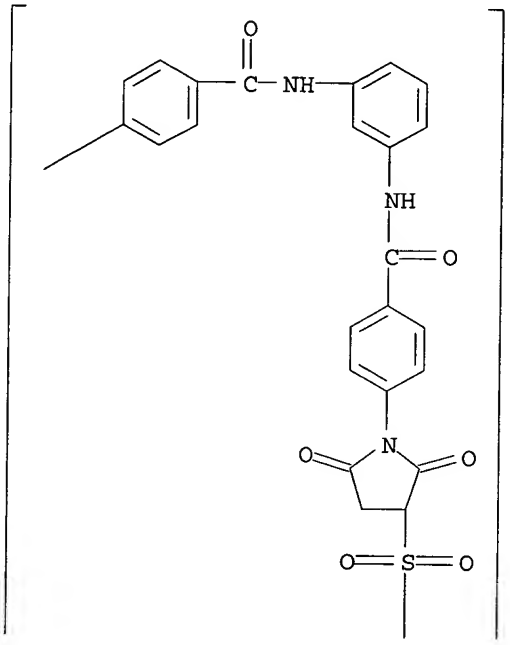
and NMR spectra with those of model compound, N-phenyl-2-phenylsulfonylsuccinimide [58534-77-3]. The polymers gave cast films with poor flexibility and had slightly better heat resistance than aliphatic polysulfone-imides.

IT **58525-20-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 58525-20-5 HCAPLUS

CN Poly[(2,5-dioxo-1,3-pyrrolidinediyl)sulfonyl-1,4-phenyleneoxy-1,4-phenylenesulfonyl(2,5-dioxo-3,1-pyrrolidinediyl)-1,4-phenylenecarbonylimino-1,3-phenyleneiminocarbonyl-1,4-phenylene] (9CI) (CA INDEX NAME)

PAGE 1-A



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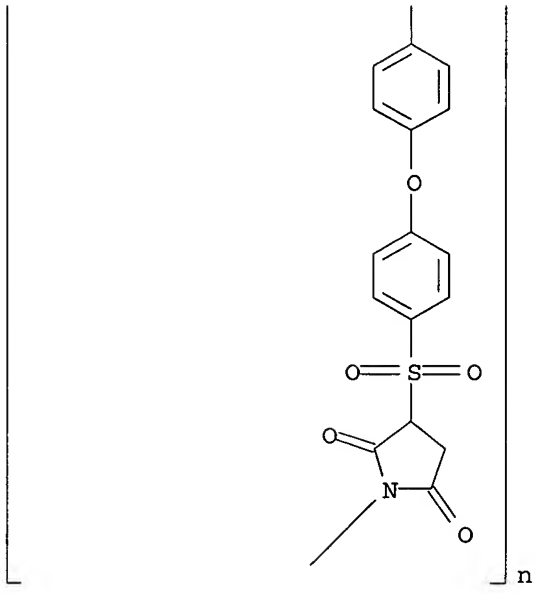


L11 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1955:49470 HCAPLUS
DOCUMENT NUMBER: 49:49470
ORIGINAL REFERENCE NO.: 49:9615i,9616a-f
TITLE: Itaconic acid derivatives of 4-aminophenyl (alkyl or aryl) sulfone
AUTHOR(S): Paytash, Peter L.; Thompson, Malcolm J.; Clarke, Wilbur B.
CORPORATE SOURCE: Xavier Univ., New Orleans, LA, USA
SOURCE: Journal of the American Chemical Society (1954), 76, 3500-1
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English

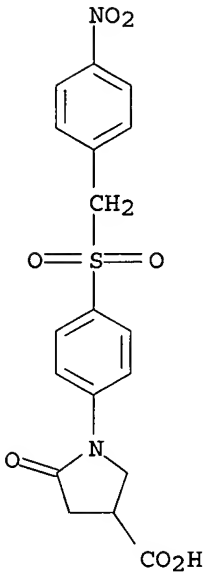
AB cf. C.A. 47, 9288g. Itaconic acid (I) can condense with alkyl or aryl 4-aminophenyl sulfones in 2 different ways to form 1-[(p-alkyl or arylsulfonyl)phenyl]-5-oxo-3-pyrrolidinecarboxylic acid (II) and 2-methylene-4'-(alkyl or arylsulfonyl)succinanilic acid (III). Both II and III were synthesized by an alternate method. Crude 1-[(p-chlorosulfonyl)phenyl]-5-oxo-3-pyrrolidinecarboxylic acid (50 g.) treated with 30 g. anhydrous $NaSO_3$ in H_2O while maintaining an alkaline reaction with $NaHCO_3$, and the resulting Na salt treated with dilute HCl yielded 35 g. 1-[(p-sulfino)phenyl]-5-oxo-3-pyrrolidinecarboxylic acid (IV), m. 175-80°. IV (10 g.) refluxed in 75 cc. 50% aqueous EtOH with 1 mole equivalent alkyl or aryl halide while maintaining an alkaline reaction with solid $NaHCO_3$, the mixture acidified with dilute HCl, and the crystalline precipitate recrystd. from H_2O or aqueous EtOH gave the corresponding II; method A. The appropriate alkyl or aryl 4-aminophenyl sulfone (V) (0.02 mole) added to 5 g. I, the mixture heated 15 min. at 180°, poured hot into cold H_2O, and the resulting precipitate of II and III hydrolyzed with acid gave the corresponding stable II; method B. By these 2 methods were prepared the following II

(p-alkyl or aryl group, % yield by method A, % yield by method B, and m.p. given): Me, 70, 15, 209-10°; Et, 62, 13, 240-2°; Pr, 75, 16, 205-6°; Bu, 80, 13, 167-8°; Am, 63, 20, 159-60°; iso-Am, 59, 20, 173-5°; C6H13, 40, 17, 154-5°; CH2:CHCH2, 50, -, 196-8°; HO2CCH2 (VI), 49, -, 203-5°; HO2C(CH2)2, 55, -, 213-15° (also 222-4°); NC(CH2)2, 85, -, 195-7° [from the K salt of IV with Cl(CH2)2CN at 44° during 48 hrs.]; EtO2CCH2, 37, -, 216-18° (dissolved in aqueous NaHCO3 and repptd. with dilute HCl) (readily hydrolyzed to VI); cyclohexylethyl, 50, -, 167-8°; PhCH2, 85, 13, 227-9°; p-O2NC6H4CH2, 80, 11, 236-8°; Ph(CH2)2, 60, -, 185-7°; p-O2NC6H4, -, 14, 215-16°; 2,4-(O2N)2C6H3, 55, 15, 145-7°; 1-phenyl-5-oxo-3-carboxypyrrolidyl, -, 10, 297-300° (decomposition). Itaconic anhydride (3 g.) condensed with 0.019 mole appropriate V by refluxing 30-45 min. in 15.0 cc. Me2CO or EtAc, the mixture poured into cold H2O, the precipitate dissolved in aqueous NaHCO3, the solution treated with C and acidified with dilute HCl, and the precipitate recrystd. from aqueous EtOH gave the corresponding III; method C. V (0.026 mole) added at 180° to 5 g. molten I, the mixture kept 2 min. at 180° and poured into cold H2O, and the precipitate purified in the usual manner gave the corresponding III; method D. By these 2 methods were prepared the following III (alkyl or aryl group, % yield by method C, % yield by method D, and m.p. given): Me, 54, 14, 191-2° (also 186-7°); Et, 53, 13, 161-2°; Pr, 56, 14, 141-2°; Bu, 55, 16, 146-7°; Am, 49, 19, 144-6°; iso-Am, 53, 20, 157-8°; C6H13, 55, 15, 143-4°; HO2CCH2, 30, -, 197-9°; NC(CH2)2, 59, -, 196-7°; EtO2CCH2, 62, -, 179-80°; PhCH2, 39, 12, 180-1°; p-O2NC6H4, 43, 9, 201-2°; BzCH2, 45, 10, 190-2°; 2,4-(O2N)2C6H3, 20, 7, 195-7°; and 4',4'''-sulfonyldi(2-methylenesuccinanilic acid), 35, -, 196-8°.

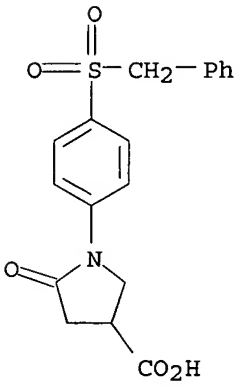
IT **857424-17-0**, 3-Pyrrolidinecarboxylic acid, 1-[p-(p-nitrobenzylsulfonyl)phenyl]-5-oxo- **857424-61-4**, 3-Pyrrolidinecarboxylic acid, 1-[p-(benzylsulfonyl)phenyl]-5-oxo- (preparation of)

RN 857424-17-0 HCAPLUS

CN 3-Pyrrolidinecarboxylic acid, 1-[p-(p-nitrobenzylsulfonyl)phenyl]-5-oxo- (5CI) (CA INDEX NAME)



RN 857424-61-4 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[p-(benzylsulfonyl)phenyl]-5-oxo- (5CI) (CA INDEX NAME)



L11 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1953:54805 HCAPLUS
DOCUMENT NUMBER: 47:54805
ORIGINAL REFERENCE NO.: 47:9288g-i,9289a-g
TITLE: Itaconic acid derivatives of sulfanilamide
AUTHOR(S): Paytash, Peter L.; Thompson, Malcolm J.; Fykes, Maurice E.
CORPORATE SOURCE: Xavier Univ., New Orleans, LA, USA
SOURCE: Journal of the American Chemical Society (1952), 74, 4549-52
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 47:54805

GI For diagram(s), see printed CA Issue.

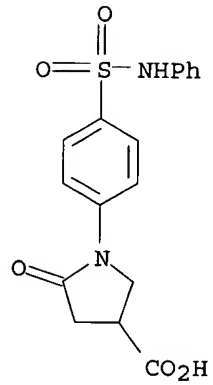
AB Fusion of itaconic acid (I) and sulfanilamides (II) gave only in some isolated cases the desired 1-(p-sulfamylphenyl)-5-oxo-3-pyrrolidinecarboxylic acid derivs. (III), which were, however, readily obtained from 1-[p-(chlorosulfonyl)phenyl]-5-oxo-3-pyrrolidinecarboxylic acid (IV) and primary and secondary amines. In the other cases the products of the fusion reaction were the p-HO2CCH2C(:CH2)CONHC6H4SO2NRR' (V), which are not intermediates in the formation of III. The V could be separated from the III by acid or base hydrolysis, which cleaved the V into I and II, but left the III unattacked. To 5 g. I heated to 180° was added in 1 portion 2 g. of the appropriate II, the mixture heated 2-5 min. to refluxing, cooled, refluxed 2 hrs. with 40 cc. 6N NaOH, cooled, acidified with dilute HCl, made alkaline with Na2CO3, filtered, the clear filtrate treated with activated C, acidified, and the resulting III purified by recrystn. from dilute alc., dilute AcOH, or dilute HCl. To 150 g. ClSO3H was added slowly with stirring at 60-5° 40 g. 1-phenyl-5-oxo-3-pyrrolidinecarboxylic acid, the mixture stirred 15-20 min. at 65-70°, and the sirupy liquid cooled to room temperature and poured slowly with stirring into a large excess of crushed ice precipitating 45-50 g. (76-85%) IV, m. 164-6°. IV was condensed with primary and secondary amines in aqueous NaHCO3 or Me2CO. By these procedures were prepared the following compds. (VI) [R = H; R', yield (%), and m.p. given]: Me, 49, 204-6°; Et, 46, 198-9°; iso-Pr, 81, 190-1°; MeO(CH2)3, 37, 104-6°; iso-PrO(CH2)3, 60, 105-7°; Bu, 51, 168-9°; cyclohexyl, 83, 174-5°; Me3CCH2CHMeCH2, 75, 185-6°; Me3CCH2CHMe(CH2)2, 35, 156-7°; HO2CCH2, 35, 190-2°; Ph, 67, 192-3°; o-ClC6H4, 57, 166-8°; m-ClC6H4, 85, 233-5°; 2,4-Cl2C6H3, 75, 210-11°; 2,5-Cl2C6H3, 65, 104-6°; o-O2NC6H4, 30, 189-91°; m-O2NC6H4, 85, 233-5°; p-O2NC6H4, 60, 220-6° (decomposition); o-MeC6H4, 65, 160-1°; m-MeC6H4, 68, 178-9°; p-MeC6H4, 41, 150-1°; 4,3-Me(O2N)C6H3, 30, 156-7°; PhCH2, 47, 194-5°; Ph(CH2)2,92, 187-8°; o-MeOC6H4, 77, 182-3°; 5,2-Cl(MeO)C6H3, 86, 188-9°; 2,5-(MeO)2C6H3, 90, 157-8°; 2,5-(EtO)2C6H3, 49, 159-60°; 3,4-(MeO)C6H3(CH2)2, 68, 114-15°; o-PhC6H4, 50, 199-200°; p-PhC6H4, 75, 214-15°; -C6H4- [the bis compound from p-C6H4(NH2)2], 80, 280° (decomposition); -C6H4C6H4- (bis compound from benzidine), 80, 315-20° (decomposition); p-(PhN:N)C6H4, 75, 252-4°; 1-C10H7, -, 192-3°; o-HO2CC6H4, 18, 218-20° (decomposition); m-HO2CC6H4, 24, 228-30°; p-HO2CC6H4, 30, 245° (decomposition); and the following VI (R and R' given): Me, Me, 70, 220-3°, 237-9°; Et, Et, 51, 152-3°; Bu, Bu, 48, 74-6°; and Et, Ph, 72, 188-9°. By the 1st procedure described were prepared from I and the appropriate II the following p-(RR'N)O2SC6H4NHCOCH2C(:CH2)CO2H [or p-(RR'N)O2SC6H4NHCOC(:CH2)CH2CO2H] (VII) (R = H, R' given): H, 5, 198-9°; Me, 31, 188-9°; Et, 23, 185-6°; iso-Pr, 53, 210-11°; MeO(CH2)3, 7, 168-9°; iso-PrO(CH2)3, 36, 174-5°; Bu, 60, 183-4°; cyclohexyl, 40, 120-2°; Me3CCH2CHMeCH2, 29, 163-4°; Me3CCH2CHMe(CH2)2, 10, 156-7°; Ph, 15, 179-80°, 183-4° (double m.p.); o-ClC6H4, 37, 197-8°; m-ClC6H4, 36, 184-5°; p-ClC6H4, 36, 208-9°; 2,4-Cl2C6H3, 37, 189-90°; 2,5-Cl2C6H3, 41, 177-8°; o-O2NC6H4, 2, 175-6°; m-O2NC6H4, 1, 179-80°; p-O2NC6H4, 3, 210-11°; o-MeC6H4, 31, 184-5°; m-MeC6H4, 30, 189-90°; p-MeC6H4, 53, 213-14°; 4,3-Me(O2N)C6H3, 4, 162-3°; PhCH2, 20, 186-8° (decomposition); Ph(CH2)2, 57, 180-1°; o-MeOC6H4, 4, 162-3° (decomposition); p-MeOC6H4, 35, 193-4°; 5,2-Cl(MeO)C6H3, 37, 172-3°; 2,5-(MeO)2C6H3, 8, 82-3°; 2,5-(EtO)2C6H3, 10, 167-8°; 3,4-(MeO)2C6H3(CH2)2, 7, 157-8°; o-PhC6H4, 15,

191-2°; p-PhC6H4, 20, 217-18°; -C6H4- [from bis(sulfanilyl)-p-phenylenediamine], 15, 207-8°; 1-C10H7, 35, 175-6°, 180-2° (decomposition) (double m.p.); 2-C10H7, 30, 181-3°; o-HO2CC6H4, 25, 133-5°; m-HO2CC6H4, 40, 195-6°; p-HO2CC6H4, 54, 225-6° (decomposition); and the following VII (R and R' given): Et, Et, 40, 156-7°; Bu, Bu, 40, 120-2°; and Ph, Et, 29, 148-9°.

IT **857424-02-3**, 3-Pyrrolidinecarboxylic acid, 5-oxo-1-[p-(phenylsulfamoyl)phenyl]- **857424-11-4**, 3-Pyrrolidinecarboxylic acid, 1-[p-[(4-nitro-m-tolyl)sulfamoyl]phenyl]-5-oxo- **857424-15-8**, 3-Pyrrolidinecarboxylic acid, 1-[p-[[p-nitrophenyl]sulfamoyl]phenyl]-5-oxo- **857424-23-8**, 3-Pyrrolidinecarboxylic acid, 1-[p-[(o-methoxyphenyl)sulfamoyl]phenyl]-5-oxo- **857424-32-9**, 3-Pyrrolidinecarboxylic acid, 1-[p-(ethylphenylsulfamoyl)phenyl]-5-oxo- **857424-39-6**, 3-Pyrrolidinecarboxylic acid, 1-[p-[[o-carboxyphenyl]sulfamoyl]phenyl]-5-oxo- **857424-41-0**, 3-Pyrrolidinecarboxylic acid, 1-[p-[[m-carboxyphenyl]sulfamoyl]phenyl]-5-oxo- **857424-50-1**, 3-Pyrrolidinecarboxylic acid, 1-[p-[[m-chlorophenyl]sulfamoyl]phenyl]-5-oxo- **857424-54-5**, 3-Pyrrolidinecarboxylic acid, 1-[p-[(5-chloro-2-methoxyphenyl)sulfamoyl]phenyl]-5-oxo- **857424-56-7**, 3-Pyrrolidinecarboxylic acid, 1-[p-[[p-carboxyphenyl]sulfamoyl]phenyl]-5-oxo- **857424-58-9**, 3-Pyrrolidinecarboxylic acid, 1-[p-[[2,4-dichlorophenyl]sulfamoyl]phenyl]-5-oxo- **857424-59-0**, 3-Pyrrolidinecarboxylic acid, 1,1'-[4,4'-biphenylenebis(iminosulfonyl-p-phenylene)]bis[5-oxo- **857424-94-3**, 3-Pyrrolidinecarboxylic acid, 1-[p-[[o-chlorophenyl]sulfamoyl]phenyl]-5-oxo- **857424-99-8**, 3-Pyrrolidinecarboxylic acid, 5-oxo-1-[p-[p-tolylsulfamoyl]phenyl]- **857425-02-6**, 3-Pyrrolidinecarboxylic acid, 5-oxo-1-[p-[o-tolylsulfamoyl]phenyl]- **857425-04-8**, 3-Pyrrolidinecarboxylic acid, 5-oxo-1-[p-[m-tolylsulfamoyl]phenyl]- **857425-08-2**, 3-Pyrrolidinecarboxylic acid, 1-[p-[[m-nitrophenyl]sulfamoyl]phenyl]-5-oxo- **857425-09-3**, 3-Pyrrolidinecarboxylic acid, 1-[p-[[o-nitrophenyl]sulfamoyl]phenyl]-5-oxo- **857425-10-6**, 3-Pyrrolidinecarboxylic acid, 1-[p-[(2,5-dimethoxyphenyl)sulfamoyl]phenyl]-5-oxo- **857425-13-9**, 3-Pyrrolidinecarboxylic acid, 5-oxo-1-[p-[(p-phenylazophenyl)sulfamoyl]phenyl]- **857425-14-0**, 3-Pyrrolidinecarboxylic acid, 1-[p-[[2,5-dichlorophenyl]sulfamoyl]phenyl]-5-oxo- **857425-18-4**, 3-Pyrrolidinecarboxylic acid, 1,1'-[p-phenylenebis(iminosulfonyl-p-phenylene)]bis[5-oxo- **857425-25-3**, 3-Pyrrolidinecarboxylic acid, 1-[p-[2-biphenylylsulfamoyl]phenyl]-5-oxo- **857425-27-5**, 3-Pyrrolidinecarboxylic acid, 1-[p-[4-biphenylylsulfamoyl]phenyl]-5-oxo- (preparation of)

RN 857424-02-3 HCAPLUS

CN 3-Pyrrolidinecarboxylic acid, 5-oxo-1-[p-(phenylsulfamoyl)phenyl]- (5CI) (CA INDEX NAME)



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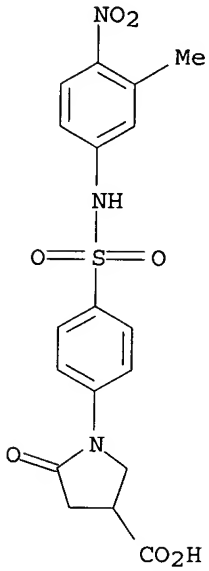

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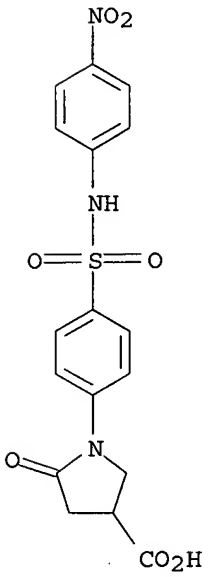

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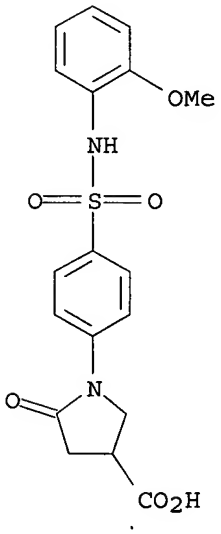

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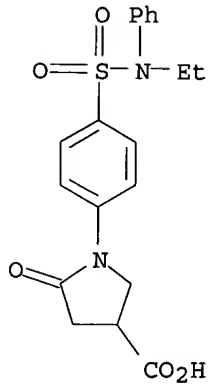

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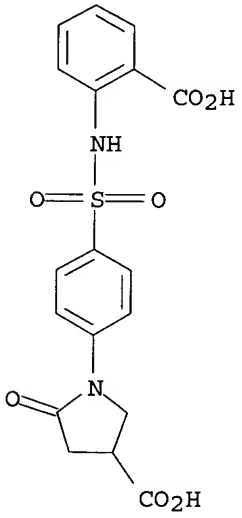

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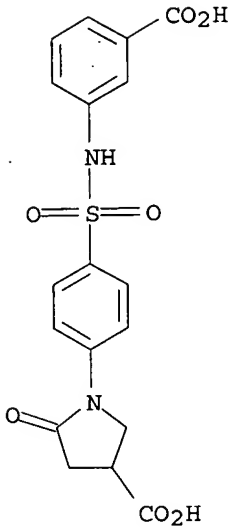

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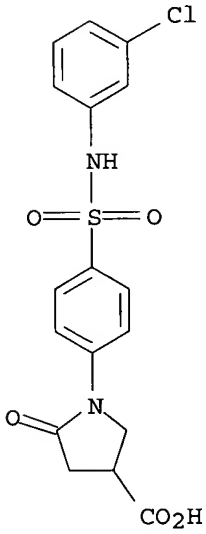

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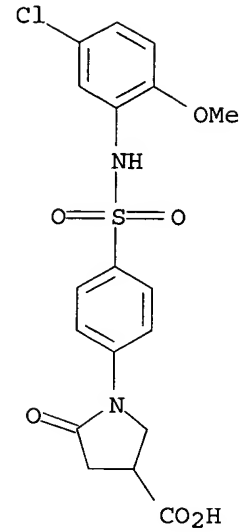

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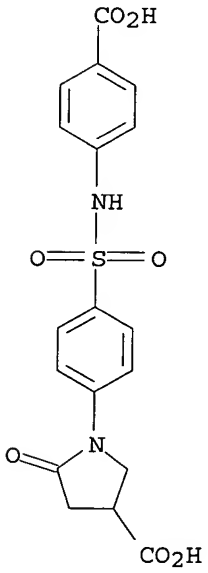

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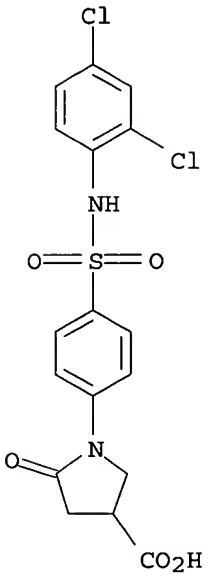

RN 857424-59-0 HCAPLUS
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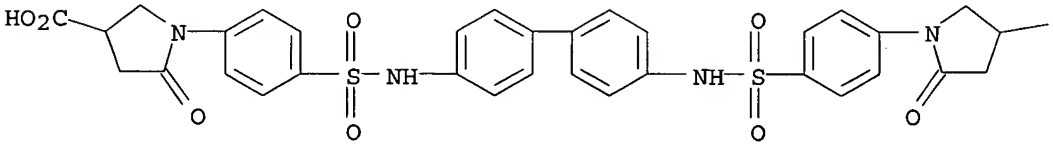
PAGE 1-A



PAGE 1-B

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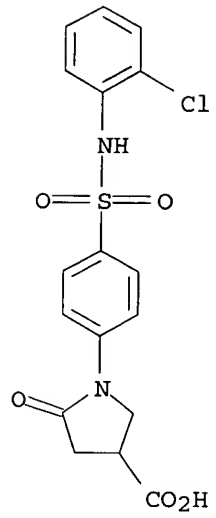

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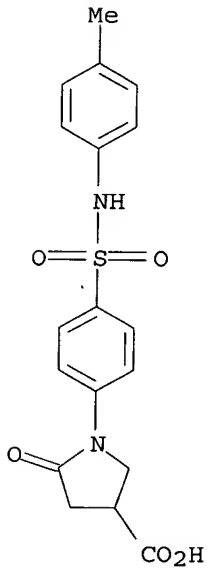

RN 857425-02-6 HCAPLUS
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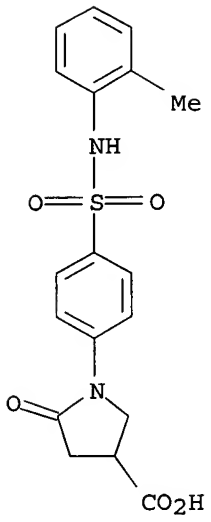
(CA INDEX NAME)



RN 857425-04-8 HCAPLUS
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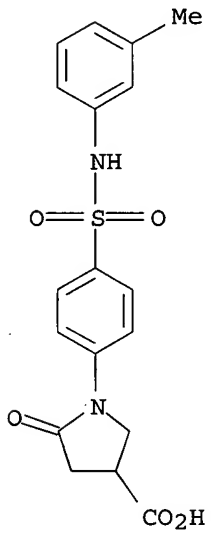

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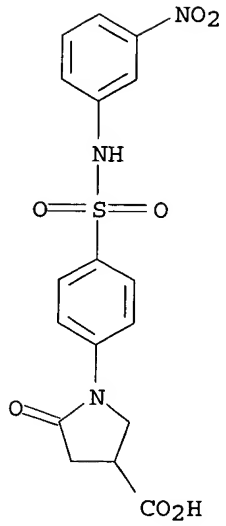

RN 857425-09-3 HCAPLUS
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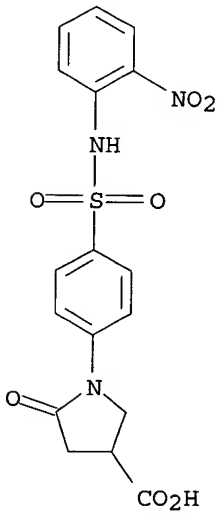
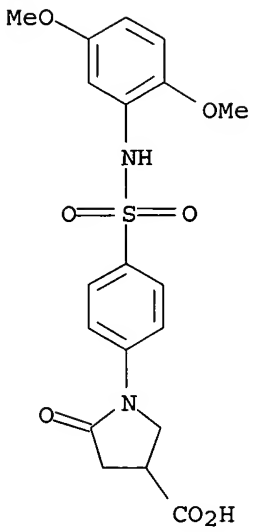


RN 857425-10-6 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[p-[(2,5-dimethoxyphenyl)sulfamoyl]phenyl]-5-oxo- (5CI) (CA INDEX NAME)



RN 857425-13-9 HCAPLUS
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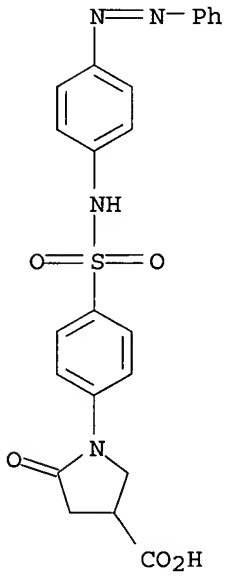

RN 857425-14-0 HCAPLUS
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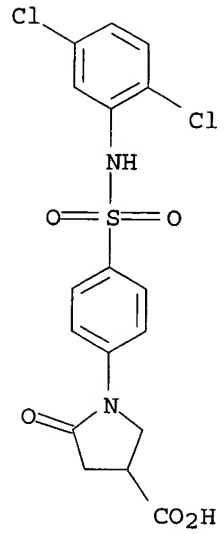

RN 857425-18-4 HCAPLUS
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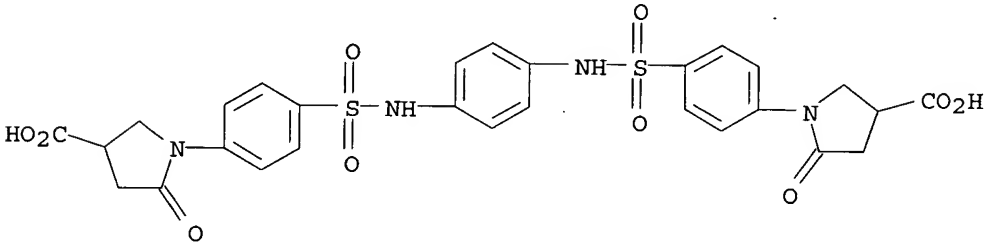

RN 857425-25-3 HCAPLUS
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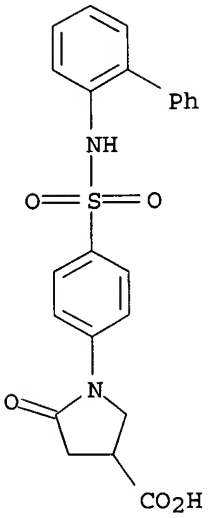
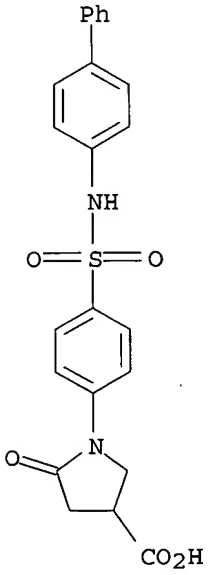


RN 857425-27-5 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 1-[p-[4-biphenylylsulfamoyl]phenyl]-5-oxo- (5CI) (CA INDEX NAME)



L11 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1950:30126 HCAPLUS
DOCUMENT NUMBER: 44:30126
ORIGINAL REFERENCE NO.: 44:5868d-i,5869a
TITLE: Reaction of itaconic acid with primary mines
AUTHOR(S): Paytash, Peter L.; Sparrow, Edward; Gathe, Joseph C.
CORPORATE SOURCE: Xavier Univ., New Orleans, LA, USA
SOURCE: Journal of the American Chemical Society (1950), 72, 1415-16
CODEN: JACSAT; ISSN: 0002-7863

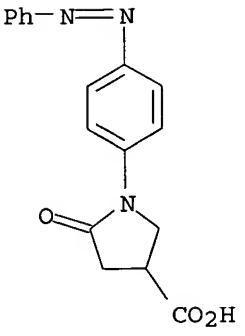
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 44:30126

AB HO2CC(:CH2)CH2CO2H, the amine, and H2O (in the ratio of 1 acid mol. to each NH2 group), refluxed 45-60 min., give the following 1-substituted 4-carboxy-2-pyrrolidones; in 32 prepns. the dry reactants were fused 10 to 20 min.; the reactions carried out in H2O are indicated. Ph (I) (H2O), m. 189-90°, 89%; o-tolyl, m. 152-3°, 62%; m-isomer, m. 129-30°, 85%; p-isomer, m. 187-8°, 88%; benzyl (H2O), m. 143-4°, 75%; cyclohexyl, m. 185-6°, 81%; (3,5,5-trimethylhexyl), m. 93-4°, 82%; anilino (H2O), m. 196-7°, 76%; (2-biphenylyl), m. 166-7°, 79%; 4-isomer, m. 249-50° (decomposition), 91%; (1-naphthyl), m. 211°, 81%; 2-isomer, m. 213°, 98%; (p-phenylazophenyl), orange, m. 242-4° (decomposition), 68%; (o-chlorophenyl), m. 144-5°, 52%; m-isomer, m. 135-6°, 84%; p-isomer, m. 150-1°, 87% (also prepared from I and SO2Cl2); (p-bromophenyl), m. 172-3°, 71% (also prepared by bromination of I in AcOH); (2-methoxy-5-chlorophenyl), m. 197-8°, 83%; (2,4-dichlorophenyl), m. 75-6°, 43% (also prepared from I and SO2Cl2); 2,5-isomer, m. 194°, 42%; (m-nitrophenyl), yellow, m. 186-7°, 61%; p-isomer, yellow, m. 175-6°, 31% (also prepared from I and HNO3); (o-hydroxyphenyl), m. 182°, 79%; m-isomer, m. 216-17°, 79%; p-isomer, m. 201-2°, 77%; (o-methoxyphenyl), m. 165°, 60%; p-isomer, m. 172-3°, 86%; (3,4-dimethoxyphenethyl), m. 129°, 77%; (m-carboxyphenyl), m. 261°, 68%; p-isomer, m. 287-8° (decomposition), 67%; (p-aminophenyl) (II) (H2O), m. 209-10° (decomposition), 72% (also prepared by reduction of the NO2 compound with Sn and HCl) [HCl salt, yellow, m. 242-5° (decomposition)]; (p-sulfamylphenyl) (III), m. 212-14°, 74% [I and ClSO3H give the sulfonyl chloride, m. 273-5° (decomposition) (165-7° on rapid heating); hydrolysis gives the sulfonic acid, m. 335-7° (decomposition); NH3 gives III]; (p-guanylsulfamylphenyl), m. 240-3° (decomposition), 61%. 1,1'-(p-Phenylene)bis(4-carboxy-2-pyrrolidone), from p-C6H4(NH2)2 m. 296-7° (decomposition), 78% (this results in 91% yield from II and HO2CC(:CH2)CH2CO2H and in 12% yield from p-C6H4(NH2)2 in H2O); 1,1'-(4,4'-biphenylene)bis(4-carboxy-2-pyrrolidone), from benzidine, m. 319-22° (decomposition), 77% (fusion of 1-(4'-amino-4-biphenylyl)-4-carboxy-2-pyrrolidone and the acid gives 83%). No reaction occurred with 2,4,6-Cl3C6H2NH2, 2,4,6-Br3C6H2NH2, 4-O2NC6H4NH2, 2,4-(O2N)2C6NH2, 2,5-(MeO)2C6H3NH2, 2-HO2CC6H4NH2, sulfathiazole, or p-H2NC6H4SO3H. The reaction therefore appears to be limited both by the nature and the position of the substituents in the amine.

IT **857425-11-7**, 3-Pyrrolidinecarboxylic acid, 5-oxo-1-(p-phenylazophenyl)-
(preparation of)

RN 857425-11-7 HCAPLUS

CN 3-Pyrrolidinecarboxylic acid, 5-oxo-1-(p-phenylazophenyl)- (5CI) (CA INDEX NAME)

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L26  ANSWER 1 OF 25  HCAPLUS  COPYRIGHT 2005 ACS on STN
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ACCESSION NUMBER: 2005:611838 HCAPLUS
DOCUMENT NUMBER: 143:115462
TITLE: Preparation of diaza-spiropiperidine derivatives for treatment of neurological and neuropsychiatric disorders
INVENTOR(S): Ceccarelli, Simona Maria; **Jolidon, Synese**; Pinard, Emmanuel; **Thomas, Andrew William**
PATENT ASSIGNEE(S): Switz.
SOURCE: U.S. Pat. Appl. Publ., 23 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005154001	A1	20050714	US 2005-28281	20050103
WO 2005068463	A1	20050728	WO 2004-EP14841	20041230

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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PRIORITY APPLN. INFO.: EP 2004-100033 A 20040108
OTHER SOURCE(S): MARPAT 143:115462
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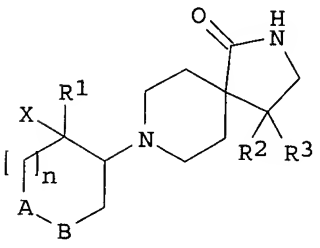

I

AB The present invention relates to compds. of formula (I) (A-B = CH2CH2, CH2O, OCH2; X = H, HO; R1 = aryl optionally substituted by one or two substituents selected from the group consisting of halogen, lower alkyl, cyano, CF3, OCF3, lower alkoxy, SO2-lower alkyl, and heteroaryl; R2 = aryl optionally substituted by one or two substituents selected from the group consisting of halogen, lower alkyl, CF3, and lower alkoxy; R3 = H, lower alkyl; n = 0-2) or pharmaceutically active salts thereof. These compds. are good inhibitors of the glycine transporter 1 (GlyT-1), and have a good selectivity over glycine transporter 2 (GlyT-2). They are useful for the treatment of diseases related to activation of NMDA receptors via Glyt-1 inhibition, including neurol. and neuropsychiatric disorders, in

particular schizophrenia and Alzheimer's disease, or for improving cognition. For example, enantiomers of cis-4-(4-Fluorophenyl)-8-[2-(4-fluorophenyl)cyclohexyl]-2,8-diazaspiro[4.5]decan-1-one inhibited the glycine uptake in Flip-in-CHO cells transfected with mGlyT-1b cDNA (glycine transporter gene) with IC50 of 36 and 43 nM.

L26 ANSWER 2 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:611837 HCAPLUS
DOCUMENT NUMBER: 143:115461
TITLE: Preparation of diaza-spiropiperidine derivatives for treatment of neurological and neuropsychiatric disorders
INVENTOR(S): **Jolidon, Synese**; Pinard, Emmanuel; **Thomas, Andrew William**
PATENT ASSIGNEE(S): Switz.
SOURCE: U.S. Pat. Appl. Publ., 30 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005154000	A1	20050714	US 2005-28125	20050103
WO 2005068462	A1	20050728	WO 2004-EP14840	20041230

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PRIORITY APPLN. INFO.: EP 2004-100034 A 20040108
OTHER SOURCE(S): MARPAT 143:115461
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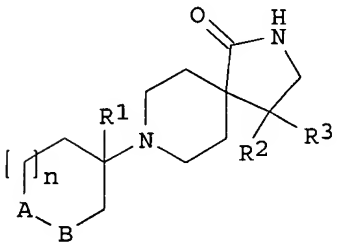

I

AB The present invention relates to compds. of formula (I) [wherein A-B = CH2CH2, CH2O, OCH2, CH2S, SCH2, CH2C(O), C(O)CH2, N(R4)CH2, CH2N(R4); R1 = lower alkyl, lower alkenyl, cycloalkyl, or aryl (optionally substituted by one or two substituents selected from the group consisting of halogen, cyano, lower alkyl, CF3, OCF3 and lower alkoxy), heteroaryl (optionally substituted by one or two substituents selected from the group consisting

of halogen, lower alkyl, CF3 and lower alkoxy); R2 = lower alkyl, cycloalkyl, aryl (optionally substituted by one or two substituents selected from the group consisting of halogen, lower alkyl, CF3, and lower alkoxy), heteroaryl (optionally substituted by one or two substituents selected from the group consisting of halogen, lower alkyl, CF3 and lower alkoxy); R3 = H, lower alkyl, benzyl; R4 = H, benzyl; n = 0, 1, 2] or pharmaceutically acceptable salts thereof. These compds. are inhibitors of glycine transporters and are useful in the treatment of neurol. and neuropsychiatric disorders, in particular schizophrenia or Alzheimer's disease, or for improving cognition or reducing pain. For example, (R)- and (S)-4-(4-Fluorophenyl)-8-[1-(4-fluorophenyl)cyclohexyl]-2,8-diazaspiro[4.5]decan-1-one inhibited the glycine uptake in Flip-in-CHO cells transfected with mGlyT-1b cDNA (glycine transporter gene) with IC50 of 56 and 73 nM vs. 103 nM for the racemate.

L26 ANSWER 3 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:395109 HCAPLUS
DOCUMENT NUMBER: 142:447129
TITLE: Preparation of benzyloxybenzazepines as monoamine oxidase-B (MAO-B) inhibitors
INVENTOR(S): **Jolidon, Synese**; Rodriguez Sarmiento, Rosa Maria; **Thomas, Andrew William**; **Wostl, Wolfgang**; **Wyler, Rene**
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005039591	A1	20050506	WO 2004-EP11541	20041014
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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US 2005107360	A1	20050519	US 2004-967567	20041018
PRIORITY APPLN. INFO.:			EP 2003-24297 A	20031023
OTHER SOURCE(S):	MARPAT 142:447129			

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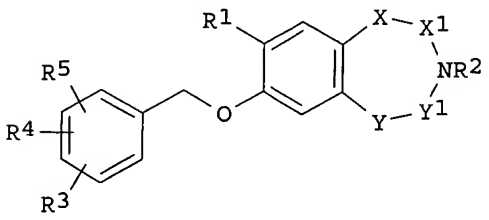


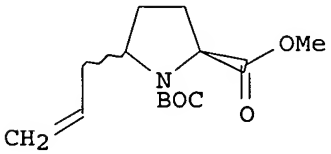
I

AB Title compds. [I; R1 = H, Me; R2 = H, alkyl, CH2CONH2, CHMeCONH2, SO2Me, COR6; R3-R5 = H, halo, cyano, alkyl, alkoxy; R6 = H, Me, CH2OMe, CONH2, CH2CONH2, OMe, NH2, NHEt; XX1, YY1 = CH2CH2, CH:CH, CH2CO; or XX1 = CH2, YY1 = CH2CH2CO; with provisos], were prepared Thus, Ac2O and HCO2H were stirred 2 h at 60°; the mixture was cooled to room temperature, diluted with THF, and 7-(3-fluorobenzyloxy)-2,3,4,5-tetrahydro-1H-benzo[d]azepine in THF/CH2Cl2 was added followed by stirring for 1 h to give 82% 7-(3-fluorobenzyloxy)-2,3,4,5-tetrahydro-1H-benzo[d]azepine-3-carboxaldehyde. The latter inhibited human MAO-B with IC50 = 0.007 μM.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 4 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:44322 HCAPLUS
DOCUMENT NUMBER: 142:280005
TITLE: Separation of pyrrolidine allylation products by diastereoselective enzymatic ester hydrolysis
AUTHOR(S): Aggarwal, Varinder K.; Astle, Christopher J.; **Iding, Hans; Wirz, Beat;** Rogers-Evans, Mark
CORPORATE SOURCE: School of Chemistry, Bristol University, Bristol, BS8 1TS, UK
SOURCE: Tetrahedron Letters (2005), 46(6), 945-947
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:280005
GI



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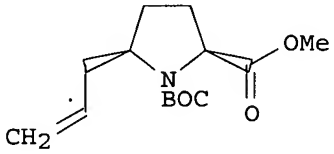

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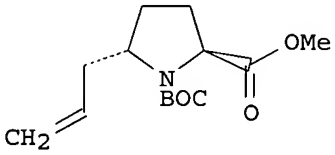


III

AB A multi-parallel enzyme screen has been used to identify potential catalysts for the selective hydrolysis of diastereomeric esters. These were subsequently applied in their separation upon scaleup. Thus, treating a cis/trans mixture of diastereomers of pyrrolidinecarboxylate I, formed in the allylation reaction, with Candida lipolytica esterase, resulted in a highly selective hydrolysis of the trans diastereomer allowing the trans carboxylic acid to be washed out in the aqueous phase leaving highly pure cis II in excellent yield (86 % of theor.). Treating the same mixture of diastereomers with R. miehei lipase resulted in a less selective ester hydrolysis, with 52 % of the trans ester III being recovered, after the cis diastereomer had been completely hydrolyzed.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 5 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:940651 HCAPLUS
DOCUMENT NUMBER: 142:336053
TITLE: The synthetic development of the anti-influenza neuraminidase inhibitor oseltamivir phosphate (Tamiflu): A challenge for synthesis & process research
AUTHOR(S): Abrecht, Stefan; Harrington, Peter; **Iding, Hans**; Karpf, Martin; Trussardi, Rene; **Wirz, Beat**; Zutter, Ulrich
CORPORATE SOURCE: Synthesis and Process Research, Basel, CH-4070, Switz.
SOURCE: Chimia (2004), 58(9), 621-629
CODEN: CHIMAD; ISSN: 0009-4293
PUBLISHER: Swiss Chemical Society
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The evolution of the synthesis of oseltamivir phosphate (Tamiflu), used for the oral treatment and prevention of influenza virus infections (viral flu) is reviewed. Oseltamivir phosphate is the Et ester prodrug of the corresponding acid, a potent and selective inhibitor of influenza neuraminidase. The discovery chemical route and scalable routes used for kilo laboratory production as well as the tech. access to oseltamivir phosphate from (-)-shikimic acid proceeding via a synthetically well-developed epoxide building block followed by azide transformations are reviewed. Synthesis and process research investigations towards azide-free conversions of the key epoxide building block to oseltamivir phosphate are discussed. The search for new routes to oseltamivir phosphate independent of shikimic acid including Diels-Alder approaches and transformations of aromatic rings employing a desymmetrization concept are presented in view of large-scale production requirements.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 6 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:809811 HCAPLUS
DOCUMENT NUMBER: 143:45241
TITLE: Protease-catalyzed preparation of (S)-2-[(tert-butylsulfonyl)-methyl]-hydrocinnamic acid for renin inhibitor RO0425892
AUTHOR(S): **Wirz, Beat**; Doswald, Stephan; Kupfer, Ernst; **Wostl, Wolfgang**; Weisbrod, Thomas; Estermann, Heinrich
CORPORATE SOURCE: F. Hoffmann-La Roche Ltd, Basel, CH-4070, Switz.
SOURCE: Asymmetric Catalysis on Industrial Scale (2004), 385-398. Editor(s): Blaser, Hans-Ulrich; Schmidt, Elke. Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, Germany.
CODEN: 69FWZH; ISBN: 3-527-30631-5
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review on protease-catalyzed reaction for the large-scale preparation of (S)-2-[(tert-butylsulfonyl)-methyl]hydrocinnamic acid (S)-3, a chiral building block in the synthesis of renin inhibitor RO0425892 (1, remikiren). The corresponding racemic Et ester substrate 2 is emulsified at elevated temperature in 20-30% concentration in an aqueous buffer and hydrolyzed enantioselectively (E>100) using cheap com. Subtilisin Carlsberg. The

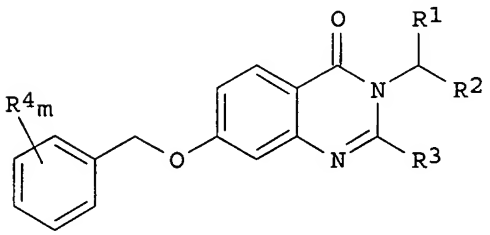
desired acid (S)-3 is separated from the remaining antipodal ester (R)-2 by repetitive extraction at alkaline and acidic pH to give the product in >99% ee and 42% yield. Awkward emulsion problems encountered with these highly concentrated reaction mixts. made the extractive work-up the most critical issue and suggested the application of a disk separator. The development of the reaction from process research to the pilot-scale is described.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 7 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:534181 HCAPLUS
DOCUMENT NUMBER: 141:89098
TITLE: Preparation of 3H-quinazolin-4-one derivatives as selective monoamine oxidase B inhibitors
INVENTOR(S): Rodriguez, Sarmiento Rosa Maria; **Thomas, Andrew William**; **Wyler, Rene**
PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004054985	A1	20040701	WO 2003-EP13888	20031208
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2509633	AA	20040701	CA 2003-2509633	20031208
EP 1572666	A1	20050914	EP 2003-789170	20031208
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2004142951	A1	20040722	US 2003-734949	20031213
PRIORITY APPLN. INFO.:			EP 2002-27700 A	20021213
			WO 2003-EP13888 W	20031208

OTHER SOURCE(S): MARPAT 141:89098
GI



I

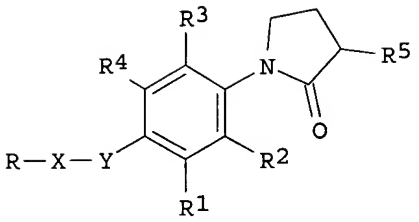
AB Title compds. I (R1 = aminocarbonylalkyl, carboxyalkyl, alkoxycarbonylalkyl, cyanoalkyl, hydroxyalkyl, alkoxyalkyl, Ph, etc.; R2 = H, halo, alkyl; R3 = H, alkyl, cycloalkyl, benzyl; R4 = halo, fluoroalkyl, cyano, alkoxy, fluoroalkoxy; m = 1, 2, 3) and their pharmaceutically acceptable salts are prepared I are useful for the treatment of Alzheimer's disease and senile dementia. Formulations containing I were given.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 8 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:267295 HCAPLUS
DOCUMENT NUMBER: 140:287260
TITLE: Preparation of 4-pyrrolidinophenyl benzyl ether derivatives as monoamine oxidase B inhibitors
INVENTOR(S): **Jolidon, Synese**; Rodriguez-Sarmiento, Rosa Maria; **Thomas, Andrew William**; **Wostl, Wolfgang**; **Wyler, Rene**
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026826	A1	20040401	WO 2003-EP10383	20030918
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2498335	AA	20040401	CA 2003-2498335	20030918
US 2004097578	A1	20040520	US 2003-666594	20030918
US 2004106650	A1	20040603	US 2003-667088	20030918
US 2004116707	A1	20040617	US 2003-667087	20030918
EP 1542971	A1	20050622	EP 2003-757866	20030918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003014314	A	20050726	BR 2003-14314	20030918
PRIORITY APPLN. INFO.:			EP 2002-21319 A	20020920
			WO 2003-EP10383 W	20030918

OTHER SOURCE(S): MARPAT 140:287260
GI



I

AB Title compds. I [R = (un)substituted Ph; X-Y = CH2CH2, CH:CH, CH2O; R1-R3 = H, halogen; R4 = H, halogen, Me; R5 = (un)substituted CONH2, NH2] were prepared for use in the prevention and treatment of illness mediated by monoamine oxidase B, in particular Alzheimer's disease or senile dementia (no data). Thus, 4-PhCH2OC6H4NH2 was treated with BrCH2CH2CHBrCOCl and the resulting amide cyclized with Dowex 2X10 to give 1-(4-benzyloxyphenyl)-3-bromo-2-pyrrolidinone which was treated with NaCN to give the 3-cyano analog.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 9 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:220040 HCAPLUS
DOCUMENT NUMBER: 140:253555
TITLE: Preparation of (oxazolylmethyl)indoles and analogs as PPAR activators for treatment of diabetes
INVENTOR(S): Binggeli, Alfred; **Wirz, Beat**; Grether, Uwe; Hilpert, Hans; Humm, Roland; **Iding, Hans**; Kuhn, Bernd; Maerki, Hans-Peter; Meyer, Markus; Mohr, Peter
PATENT ASSIGNEE(S): Hoffmann-La Roche Inc., Switz.
SOURCE: U.S. Pat. Appl. Publ., 39 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004053979	A1	20040318	US 2003-659664	20030910
US 6890947	B2	20050510		
CA 2494601	AA	20040325	CA 2003-2494601	20030904
WO 2004024726	A1	20040325	WO 2003-EP9819	20030904
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1539746	A1	20050615	EP 2003-747962	20030904
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003014261	A	20050726	BR 2003-14261	20030904

PRIORITY APPLN. INFO.: EP 2002-20477 A 20020912
WO 2003-EP9819 W 20030904

OTHER SOURCE(S): MARPAT 140:253555
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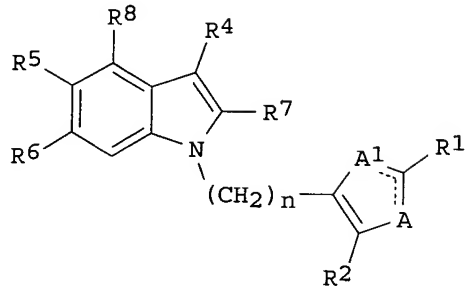

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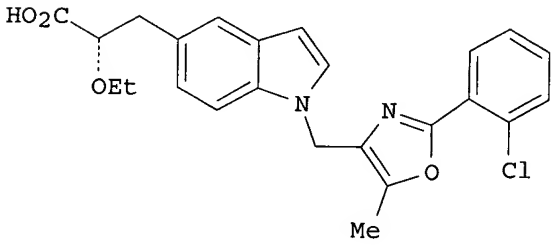


II

AB Title compds. I [wherein R1 = (hetero)aryl; R2, R4, R7, and R8 = independently H or (cyclo)alkyl; R3 = (halo)aryloxy or (halo)alkenyloxy; any one of R5 and R6 = C=CR3CO2H or CHCHR3CO2H and the other is H or (cyclo)alkyl; any one of A and A1 = N and the other is O or S; n = 1-3; or a pharmaceutically acceptable salt or ester thereof] were prepared as Peroxisome proliferator activated receptor (PPAR) agonists. For example, (S)-2-ethoxy-3-(1H-indol-5-yl)propionic acid Me ester was coupled with 4-chloromethyl-2-(2-chlorophenyl)-5-methyloxazole using KOH in DMSO to give II (56%). In radioligand binding assays against PPARα and PPARγ, II exhibited IC50 values of 0.24 μM and 0.36 μM, resp., and EC50 values of 1.52 μM and 0.17 μM, resp. Thus, I and their pharmaceutical compns. are useful for the treatment of non-insulin dependent diabetes (no data).

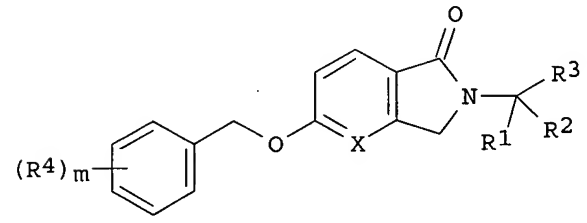
L26 ANSWER 10 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:143104 HCAPLUS
DOCUMENT NUMBER: 140:181326
TITLE: Preparation of 2,3-dihydro-isoindol-1-ones as monoamine oxidase MAO-B inhibitors.
INVENTOR(S): **Jolidon, Synese**; Rodriguez-Sarmiento, Rosa Maria; **Thomas, Andrew William**; **Wyler, Rene**
PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004014856	A1	20040219	WO 2003-EP8456	20030731
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004082603	A1	20040429	US 2003-625116	20030722
US 6846832	B2	20050125		
CA 2493143	AA	20040219	CA 2003-2493143	20030731
EP 1539694	A1	20050615	EP 2003-784117	20030731
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003013543	A	20050621	BR 2003-13543	20030731
PRIORITY APPLN. INFO.:			EP 2002-17676 A	20020807
			WO 2003-EP8456 W	20030731

OTHER SOURCE(S): MARPAT 140:181326

GI



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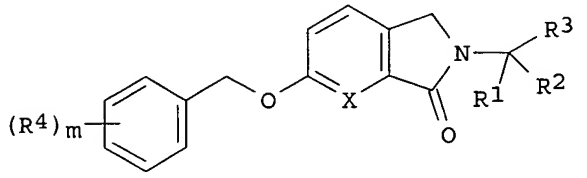


II

AB Title compds. [I, II; X = N, CH; R1 = (CH2)nCONR5R6, (CH2)nNR5R6, (CH2)nCO2R7; (CH2)nCN, (CH2)n-isoindole-1,3-dionyl, (CH2)pOR8; R2 = H, alkyl, OH; R3 = H, alkyl; R4 = halo, haloalkyl, alkoxy, haloalkoxy; R5, R6 = H, alkyl; R7 = alkyl; R8 = H, alkyl; m = 1-3; n = 0-2; p = 1, 2], were prepared Thus, 5-(3-fluorobenzyloxy)-2,3-dihydroisoindol-1-one (preparation given) and NaH were stirred in THF at room temperature for 45 min; 2-bromoacetamide was added and the resulting mixture heated at 50° for 16 h to give 67% 2-[5-(3-fluorobenzyloxy)-1-oxo-1,3-dihydroisoindol-2-yl]acetamide. Title compds. inhibited MAO-B in the range of ≤10 μM.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 11 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:60452 HCAPLUS
DOCUMENT NUMBER: 140:128156
TITLE: Preparation of cinnamide derivatives useful as selective MAO-B inhibitors
INVENTOR(S): **Jolidon, Synese**; Rodriguez, Sarmiento Rosa Maria; **Thomas, Andrew William**; **Wostl, Wolfgang**; **Wyler, Rene**
PATENT ASSIGNEE(S): F. Hoffmann-La Roche AG, Switz.
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004007429	A1	20040122	WO 2003-EP7231	20030707
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004034096	A1	20040219	US 2003-613785	20030703
US 6900354	B2	20050531		
CA 2493372	AA	20040122	CA 2003-2493372	20030707
EP 1523469	A1	20050420	EP 2003-740425	20030707
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003012658	A	20050426	BR 2003-12658	20030707
PRIORITY APPLN. INFO.:			EP 2002-15583 A	20020715
			WO 2003-EP7231 W	20030707

OTHER SOURCE(S): MARPAT 140:128156
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention refers to cinnamide derivs. of formula I [wherein: R1 = alkyl, halogen, halogenoalkyl, CN, alkoxy, halogenoalkoxy; R21, R22, R23, R24 = H or F; R3 = H, alkyl; A = -C(R4):C(R5)-, -C(R4)(R6)-C(R7)(R5)-, or -C.tplbond.C-; R4, R5, R6, R7 = H, alkyl; n = 1-3] useful for treatment and prevention of diseases mediated by MAO-B inhibitors. Compds. I are especially useful for the treatment of Alzheimer's disease and senile dementia. For instance, compound II (example 1, IC50 = 0.083 μmol for human MAO-B; >10,000 for human MAO-A) was prepared via etherification of 4-iodophenol by 3-fluorobenzyl bromide, Sonogashira reaction of CH2:C(Me)CO2Me with obtained compound III, subsequent hydrolysis and amidation.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 12 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:1013030 HCAPLUS
DOCUMENT NUMBER: 140:236033
TITLE: Chemo-enzymatic preparation of chiral 3-aminopyrrolidine derivatives
AUTHOR(S): **Iding, Hans; Wirz, Beat;** Rogers-Evans, Mark
CORPORATE SOURCE: Non-clinical Development-Biotechnology, F. Hoffmann-La Roche Ltd., Basel, Switz.
SOURCE: Tetrahedron (2004), 60(3), 647-653
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new simple method for the enantioselective enzymic hydrolysis of N-protected D-asparagine esters suitable for the use on the preparative scale is presented. Due to major obstacles observed under conventional reaction conditions-racemization of the retained ester and a strong enzyme inactivation-a comparatively low pH together with an organic co-solvent had to be employed. Under these conditions, nearly all tested proteases demonstrated good activity and excellent enantioselectivity giving access to the corresponding D-esters and L-asparagines in high optical purities (>95% ee) and good chemical yields (>40%). From the unnatural D-asparagine derivative, sequential cyclization, selective deprotection and reduction yielded efficiently benzyl protected (R)-3-aminopyrrolidine, a homo-chiral building block utilized in numerous drug candidates.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

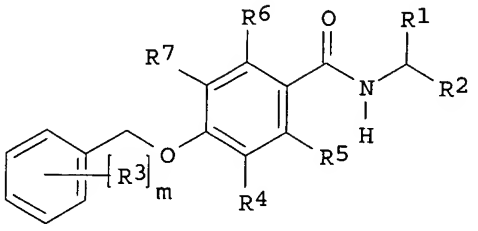
L26 ANSWER 13 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:1006920 HCAPLUS
DOCUMENT NUMBER: 140:59408
TITLE: Preparation of fluorobenzamides as monoamine oxidase B inhibitors for the treatment of treatment of Alzheimer's disease or senile dementia
INVENTOR(S): **Jolidon, Synese**; Rodriguez Sarmiento, Rosa Maria; **Thomas, Andrew William**; **Wyler, Rene**
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003106380	A2	20031224	WO 2003-EP6008	20030607
WO 2003106380	A3	20040311		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003236304	A1	20031225	US 2003-456641	20030606
US 6951884	B2	20051004		
CA 2489247	AA	20031224	CA 2003-2489247	20030607
BR 2003011719	A	20050315	BR 2003-11719	20030607
EP 1515926	A2	20050323	EP 2003-735578	20030607
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005529176	T2	20050929	JP 2004-513216	20030607
PRIORITY APPLN. INFO.:			EP 2002-12484 A	20020612
			WO 2003-EP6008 W	20030607

OTHER SOURCE(S): MARPAT 140:59408
GI



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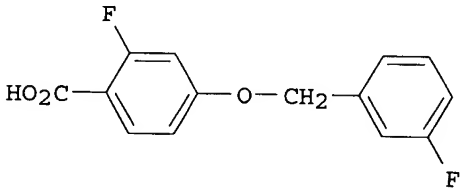

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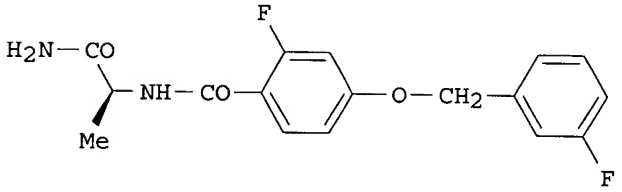


III

AB Title compds. I [R1 = H, alkyl, alkyl-OH; R2 = alkyl, CONR8R9, (CH2)nNR8R9, etc.; R3 = H, halo, haloalkyl, etc.; R4, R5, R6, R7 = H, F with the proviso that at least one of R4, R5, R6 and R7 = F; R8, R9 = H, alkyl; m = 1-3; n = 0-3] and their pharmaceutically acceptable salts and formulations were prepared For example, coupling of benzoic acid II, e.g., prepared from 2-fluoro-4-hydroxybenzonitrile in 2-steps, and L-alaninamide hydrochloride afforded fluorobenzamide III in 54% yield. In human monoamine oxidase B (MAO-B) inhibition studies, 24-examples of compds. I exhibited IC50 values ranging from 3.1-26 nM, e.g., the IC50 value of fluorobenzamide III was 5.9 nM. Compds. I are claimed useful for the treatment of Alzheimer's disease or senile dementia.

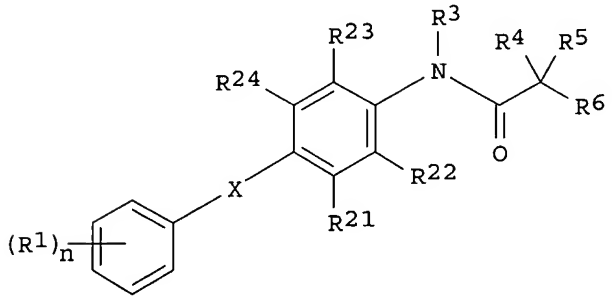
L26 ANSWER 14 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:950974 HCAPLUS
DOCUMENT NUMBER: 140:16567
TITLE: N-(Acylamino)benzene derivatives as selective monoamine oxidase B inhibitors

INVENTOR(S): **Jolidon, Synese**; Rodriguez Sarmiento, Rosa Maria; **Thomas, Andrew William**; **Wyler, Rene**
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003099763	A1	20031204	WO 2003-EP5297	20030520
WO 2003099763	C1	20040318		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2486380	AA	20031204	CA 2003-2486380	20030520
EP 1511718	A1	20050309	EP 2003-730080	20030520
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003011338	A	20050322	BR 2003-11338	20030520
JP 2005527617	T2	20050915	JP 2004-507421	20030520
US 2003232883	A1	20031218	US 2003-445580	20030527
US 6762320	B2	20040713		
US 2004210079	A1	20041021	US 2004-839514	20040505

PRIORITY APPLN. INFO.:
EP 2002-11639 A 20020529
WO 2003-EP5297 W 20030520
US 2003-445580 A1 20030527

OTHER SOURCE(S): MARPAT 140:16567
GI



I

AB Title compds. such as I (R1 = halo, haloalkyl, cyano, alkoxy, haloalkoxy; n = 0, 1, 2, 3; X = CH2O, OCH2, CH2CH2, CH:CH, C.tplbond.C, etc.; R21, R22, R23, R24 = H, alkyl, halo, haloalkyl, OH, etc.; R3 = H, alkyl; R4, R5 = H, alkyl, alkoxy, alkoxycarbonyl, etc.; R6 = CONR7R8, alkoxycarbonyl, CN, etc.; R7, R8 = H, alkyl, NH2, OH) were prepared Thus,

4-(3-FC6H4CH2O)C6H4NHCOCH2CO2Me was prepared in 3 steps starting from 3-fluorobenzyl alc. and 1-fluoro-4-nitrobenzene. Several I were selective monoamine oxidase B inhibitors and are therefore useful in the treatment of diseases such as Alzheimer's disease and senile dementia.

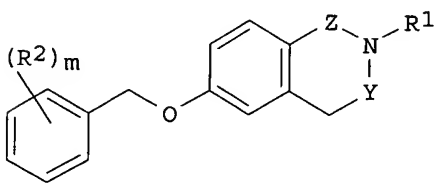
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 15 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:875255 HCAPLUS
DOCUMENT NUMBER: 139:364839
TITLE: Preparation of isoquinolines as monoamine oxidase B inhibitors useful against Alzheimer's disease and senile dementia
INVENTOR(S): Cesura, Andrea; Rodriguez Sarmiento, Rosa Maria; Scalone, Michelangelo; **Thomas, Andrew William**; **Wyler, Rene**
PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003091219	A1	20031106	WO 2003-EP3845	20030414
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2483461	AA	20031106	CA 2003-2483461	20030414
EP 1501804	A1	20050202	EP 2003-725018	20030414
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003009562	A	20050215	BR 2003-9562	20030414
US 2003225122	A1	20031204	US 2003-417378	20030416
US 6818774	B2	20041116		

PRIORITY APPLN. INFO.:
EP 2002-9253 A 20020426
WO 2003-EP3845 W 20030414

OTHER SOURCE(S): MARPAT 139:364839
GI



I

AB This invention relates to isoquinolines (shown as I; e.g. 2-[6-(3-fluorobenzyloxy)-1-oxo-3,4-dihydro-1H-isoquinolin-2-yl]acetamide; Y is C:O, or CH2; Z is C:O or CH2; R1 is H or CR3R4R5 (R3 is -(CH2)nC(O)NR6R7, -(CH2)nCOOR8, -CHR9COOR8, -(CH2)nCN, -(CH2)pOR8, -(CH2)nNR6R7, -(CH2)nCF3, -(CH2)nNHC(O)R9, -(CH2)nNHCOOR8, -(CH2)ntetrahydrofuranyl, -(CH2)pSR8, -(CH2)pS(O)R9, or -(CH2)nC(S)NR5R6; R4 is H, C1-C6-alkyl, - (CH2)pOR8, -(CH2)pSR8, or benzyl; R5 is H, C1-C6-alkyl, -(CH2)pOR8, -(CH2)pSR8, or benzyl; R6 and R7 = H or C1-C6-alkyl; R8 is H or C1-C6-alkyl; R9 is C1-C6-alkyl; m = 1-3; n = 0-2; and p = 1-2; R2 = halogen, halogen-(C1-C6)-alkyl, cyano, C1-C6-alkoxy or halogen-(C1-C6)-alkoxy)) as well as to their pharmaceutically acceptable salts. The invention further relates to medicaments containing these compds., a process for their preparation as well as their use for preparation of medicaments for the treatment or prevention of diseases in which MAO-B inhibitors might be beneficial. IC50 values for 17 examples of I against monoamine oxidase A and B are tabulated, e.g. 0.008 and 0.33 μM for 2-[6-(3-fluorobenzyloxy)-1-oxo-3,4-dihydro-1H-isoquinolin-2-yl]acetamide. Sixty example prepns. of I are included. For example, 6-(3-Fluorobenzyloxy)-3,4-dihydro-2H-isoquinolin-1-one was prepared in 3 steps (49, 65, 87 % yields) starting from 5-methoxy-1-indanone and involving intermediates 6-methoxy-3,4-dihydro-2H-isoquinolin-1-one and 6-hydroxy-3,4-dihydro-2H-isoquinolin-1-one.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 16 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:777757 HCAPLUS

DOCUMENT NUMBER: 139:292146

TITLE: Preparation of (benzyloxy)phthalimides as inhibitors of monoamine oxidase B

INVENTOR(S): Cesura, Andrea; Rodriguez Sarmiento, Rosa Maria; **Thomas, Andrew William; Wyler, Rene**

PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.

SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003080573	A1	20031002	WO 2003-EP2931	20030320
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003195208	A1	20031016	US 2003-387950	20030313
US 6660736	B2	20031209		
CA 2477771	AA	20031002	CA 2003-2477771	20030320
EP 1490334	A1	20041229	EP 2003-744825	20030320
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

BR 2003008786	A	20050111	BR 2003-8786	20030320
JP 2005526796	T2	20050908	JP 2003-578328	20030320
US 2004229871	A1	20041118	US 2003-657857	20030909
US 6903095	B2	20050607		

PRIORITY APPLN. INFO.:

EP 2002-7222	A	20020327
US 2003-387950	A3	20030313
WO 2003-EP2931	W	20030320

OTHER SOURCE(S): MARPAT 139:292146

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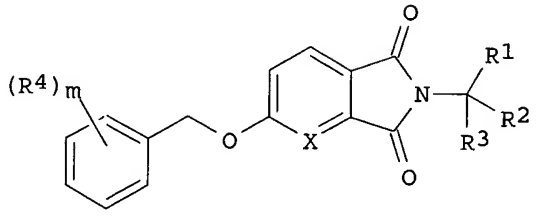

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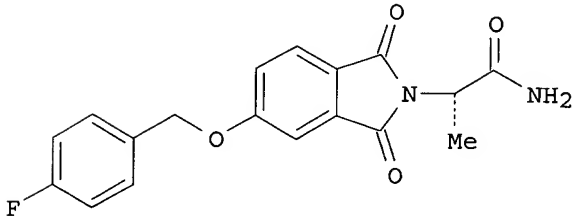

II

AB Title compds. I [wherein X = N or CH; R1 = CONR5R6, CHR7(CH2)nCONR5R6, (CH2)nNR5R6, (CH2)nCO2R8, (CH2)nCN, CHR7(CH2)nCF3, (CH2)nNHCOR9, (CH2)nNHCO2R9, (CH2)pOR8, (CH2)pSR8, (CH2)pSOR9, (CH2)nCSNR5R6, or (un)substituted (CH2)n-piperidinyl, (CH2)n-morpholinyl, (CH2)n-tetrahydrofuranyl, (CH2)n-thiophenyl, (CH2)n-isoxazolyl, (CH2)n-Ph; R2 = H, alkyl, (CH2)pOR10, (CH2)pSR10, or CH2Ph; R3, R5, R6, R8, and R10 = independently H or alkyl; R4 = H, haloalkyl, CN, or (halo)alkoxy; R7 = H, OH, or alkoxy; R9 = alkyl; m = 1-3; n = 0-2; p = 1-2; and pharmaceutically acceptable salts thereof] were prepared as highly selective monoamine oxidase B (MAO-B) inhibitors. For example, reaction of 4-hydroxyphthalic acid with 4-fluorobenzyl bromide in the presence of K2CO3 in acetone and H2O gave 4-(4-fluorobenzyloxy)phthalic acid bis(4-fluorobenzyl)ester (80%). Saponification with LiOH•H2O in THF afforded the acid (56%). Cyclocondensation with alaninamide•HCl using carbonyldiimidazole in 1-methyl-2-pyrrolidinone provided the title isoindole II (49%). The latter preferentially inhibited the enzymic activity of human MAO-B over human MAO-A with IC50 values of 0.008 μM and 0.776 μM, resp. Thus, I and their pharmaceutical compns. are useful for the treatment of diseases mediated by MAO-B, such as Alzheimer's disease and senile dementia (no data).

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 17 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:633667 HCAPLUS

DOCUMENT NUMBER: 139:179980

TITLE: Preparation of N-substituted pyridinecarboxamides as inhibitors of monoamine oxidase (MAO-B)

INVENTOR(S): Cesura, Andrea; Rodriguez Sarmiento, Rosa Maria; **Thomas, Andrew William; Wyler, Rene**

PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.

SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003066596	A1	20030814	WO 2003-EP769	20030127
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003158235	A1	20030821	US 2003-341672	20030114
US 6667327	B2	20031223		
CA 2473459	AA	20030814	CA 2003-2473459	20030127
EP 1474394	A1	20041110	EP 2003-702531	20030127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003007444	A	20041228	BR 2003-7444	20030127
JP 2005528339	T2	20050922	JP 2003-565970	20030127

PRIORITY APPLN. INFO.: EP 2002-1969 A 20020204
WO 2003-EP769 W 20030127

OTHER SOURCE(S): MARPAT 139:179980

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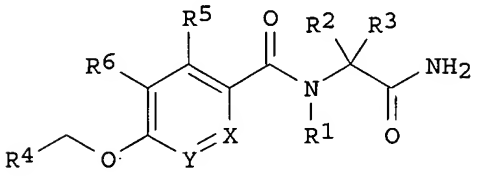


I

AB The title compds. [I; one of X or Y = N and the other one = CR7; R1-R3 = H, alkyl; R4 = haloalkyl, (un)substituted aryl; R5-R7 = H, alkyl], useful for the treatment or prevention of neurol. diseases such as Alzheimer, dementia, Parkinson's diseases and depression, were prepared and formulated. Thus, reacting 6-chloronicotinic acid with PhCH2OH in the presence of KOH in DMSO (yield 75%) followed by amidation of 6-benzyloxynicotinic acid with glycinamide.HCl (53%) afforded 6-benzyloxy-N-(carbamoylmethyl)nicotinamide which showed IC50 of 0.033 μM against MAO-B.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 18 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:405912 HCAPLUS
DOCUMENT NUMBER: 139:230550
TITLE: Chemoenzymatic preparation of non-racemic N-Boc-pyrrolidine-3,4-dicarboxylic acid 3-ethyl esters and their 4-hydroxymethyl derivatives
AUTHOR(S): Rodriguez Sarmiento, Rosa Maria; **Wirz, Beat**; **Iding, Hans**
CORPORATE SOURCE: Pharmaceutical Research Basel Discovery - Medicinal Chemistry, F. Hoffmann-La Roche Ltd., Basel, Switz.
SOURCE: Tetrahedron: Asymmetry (2003), 14(11), 1547-1551
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:230550
AB For the synthesis of metalloproteinase inhibitors, the (R,R)- and (S,S)-monoethyl esters of N-Boc-pyrrolidine-3,4-dicarboxylic acid were prepared as key intermediates from the trans-diester racemate by two consecutive, highly selective enzymic reactions. Reduction of the formed acids to the corresponding enantiopure hydroxymethyl derivs. ((R,R)- and (S,S)-Et N-Boc-4-hydroxymethyl-3-carboxylate) gives access to a new series of chiral building blocks.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

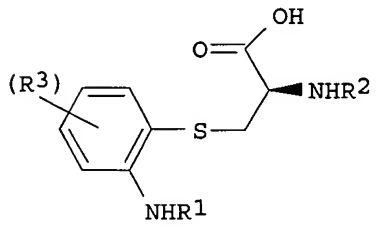
L26 ANSWER 19 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:405911 HCAPLUS
DOCUMENT NUMBER: 139:230586
TITLE: Chemoenzymatic preparation of non-racemic N-Boc-piperidine-3,5-dicarboxylic acid 3-methyl esters and their 5-hydroxymethyl derivatives
AUTHOR(S): **Iding, Hans**; **Wirz, Beat**; Rodriguez Sarmiento, Rosa-Maria
CORPORATE SOURCE: Non-clinical Development-Biotechnology, F. Hoffmann-La-Roche Ltd, Basel, Switz.
SOURCE: Tetrahedron: Asymmetry (2003), 14(11), 1541-1545
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:230586
AB For the synthesis of (R,R)- and (S,S)-N-Boc-5-hydroxymethyl-piperidine-3-carboxylic acid Me ester as important basic units for potential inhibitors of aspartyl proteases, the resp. non-racemic 3,5-dicarboxylic acid monomethyl esters were prepared as key intermediates from a cis,trans-mixture of the resp. diester by several consecutive enzymic reactions using Lipase AY, Chirazyme L-2, Hydrolase ESP-ESL-1064 and pig liver esterase.
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 20 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:282759 HCAPLUS
DOCUMENT NUMBER: 138:302750
TITLE: Enzymatic process for the preparation of substituted 2-amino-3-(2-amino-phenylsulfanyl)-propionic acid
INVENTOR(S): Bleicher, Konrad; Borthwick, Scott; **Iding, Hans**; Rogers-Evans, Mark; Schmid, Stefan; Tong, Han Min; **Wirz, Beat**
PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.

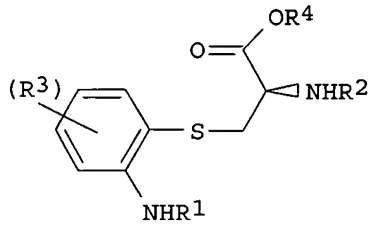
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003029477	A1	20030410	WO 2002-EP10511	20020919
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2461296	AA	20030410	CA 2002-2461296	20020919
EP 1434870	A1	20040707	EP 2002-779375	20020919
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
CN 1553959	A	20041208	CN 2002-817772	20020919
JP 2005503830	T2	20050210	JP 2003-532690	20020919
US 2003119152	A1	20030626	US 2002-252971	20020923
PRIORITY APPLN. INFO.:			EP 2001-122906 A	20010925
			WO 2002-EP10511 W	20020919

OTHER SOURCE(S): CASREACT 138:302750; MARPAT 138:302750
GI



I



II

AB The compds. of formula (I) are useful for the preparation of 1,5-benzothiazepines which are useful as enzyme inhibitors, such as protease, interleukin-1-converting enzyme, elastase or angiotensin enzyme, GPCR antagonists (cholecystokinin, angiotensin II receptor). The present invention relates to a new process for the preparation compds. of formula I, wherein R1, R2, R3 and n are as described in the description which process comprises reacting compds. of formula (II), wherein R1, R2, R3, n and R4 are as described in the description, with a protease in an aqueous system containing an organic co-solvent.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 21 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:780477 HCAPLUS

DOCUMENT NUMBER: 135:317542
TITLE: Process for the preparation of D-asparagine derivatives
INVENTOR(S): **Iding, Hans**; Rogers-Evana, Mark; **Wirz, Beat**
PATENT ASSIGNEE(S): Basilea Pharmaceutica A.-G., Switz.
SOURCE: Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1148140	A1	20011024	EP 2001-108896	20010410
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2001049127	A1	20011206	US 2001-834129	20010412
US 6420166	B2	20020716		
JP 2001309798	A2	20011106	JP 2001-120759	20010419
JP 3568914	B2	20040922		

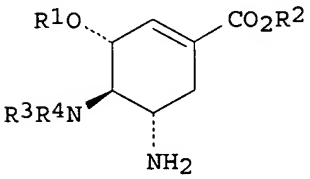
PRIORITY APPLN. INFO.: EP 2000-108542 A 20000419
OTHER SOURCE(S): CASREACT 135:317542; MARPAT 135:317542
AB The optically active D-asparagine derivs. are useful for the preparation of optically active 3-aminopyrrolidine derivs. which are important building blocks for the production of useful products in the chemical, agricultural and in the pharmaceutical industry. In particular they are useful in the production of antibacterial substances for example of vinylpyrrolidinone-cephalosporin derivs. The process may also be used for the preparation of N-protected L-asparagine by work up of the remaining aqueous layer. The present invention relates to a new process for the preparation of D-asparagine derivs. with an amino protecting group and the α-carboxy esterified by an alkyl, a substituted alkyl, or a group of formula R(OCH2CH2)n-, wherein R is H or a lower alkyl group and n is 1, 2 or 3, which process comprises reacting a racemic N-protected, esterified asparagine derivative with a protease in an aqueous system at a pH of 6.0-7.5, preferably 6.0-7.0, together with an organic co-solvent, and subsequent extraction of the enantiomeric pure D-asparagine derivative
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 22 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:760045 HCAPLUS
DOCUMENT NUMBER: 135:303728
TITLE: Preparation of tamiflu and diaminoshikimic acid derivatives, gallocarboxylic acid approach
INVENTOR(S): **Iding, Hans**; **Wirz, Beat**; Zutter, Ulrich
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: Eur. Pat. Appl., 27 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

EP 1146036	A2	20011017	EP 2001-107754	20010403
EP 1146036	A3	20030730		
EP 1146036	B1	20050323		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2001036653	A1	20011101	US 2001-811862	20010319
US 6518048	B2	20030211		
AT 291568	E	20050415	AT 2001-107754	20010403
ES 2238035	T3	20050816	ES 2001-1107754	20010403
CA 2343346	AA	20011010	CA 2001-2343346	20010406
JP 2001354635	A2	20011225	JP 2001-108136	20010406
CN 1317481	A	20011017	CN 2001-116366	20010410

PRIORITY APPLN. INFO.: EP 2000-107669 A 20000410
OTHER SOURCE(S): CASREACT 135:303728
GI



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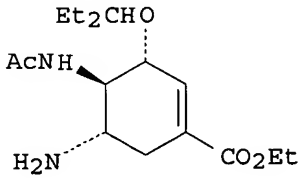
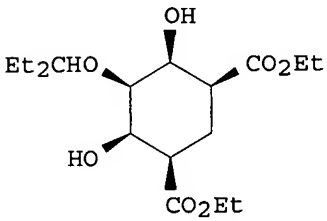
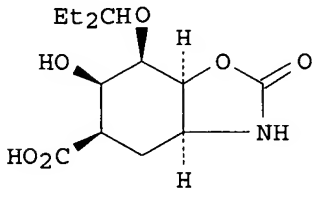


II



III

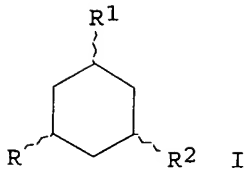


IV

AB The 4,5-diaminoshikimic acid derivs. I (R1 = optionally substituted alkyl; R2 = alkyl; R3, R4 = H or a substituent of an amino group, both R3 and R4 are not H), inhibitors of viral neuraminidase, were prepared in a multistep process starting from an isophthalic acid. Thus, the diaminocyclohexenecarboxylic acid (tamiflu, II), was prepd in 12 steps from 1-ethylpropyl methanesulfonate and 2,6-dimethoxyphenol via the isophthalic acid diester III and benzoxazole derivative II.

L26 ANSWER 23 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:836446 HCAPLUS
DOCUMENT NUMBER: 134:193619
TITLE: Multiselective enzymatic reactions for the synthesis of protected homochiral cis- and trans-1,3,5-cyclohexanetriols
AUTHOR(S): **Wirz, B.**; **Iding, H.**; Hilpert, H.
CORPORATE SOURCE: Pharmaceutical Research Basel-Biological Sciences, F. Hoffmann-La Roche Ltd, Basel, Switz.
SOURCE: Tetrahedron: Asymmetry (2000), 11(20), 4171-4178
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:193619

GI



I

AB For the synthesis of the potentially antipsoriatic vitamin D derivative, Ro 65-2299, an efficient and multiselective enzymic step was developed in which the easily accessible trans-1,3,5-triacetoxy-cyclohexane I (R = R1 = α-OAc, R2 = β-OAc) was selectively monohydrolyzed in the presence of the cis-isomer I (R = R1 = R2 = α-OAc) to give (1R,3R)-1,3-diacetoxy-5-hydroxy-cyclohexane I (R = α-OAc, R1 = α-OH, R2 = β-OAc) in high enantiomeric excess (>99%) and yield (84%). Furthermore, for the synthesis of the enantiomer of Ro 65-2299 a simple and efficient enzymic procedure for the asym. acetylation of cis-1,5-dihydroxy-3-(tert-butyldimethylsilanoxy)-cyclohexane I (R = α-OSiMe2CMe3, R1 = R2 = α-OH) in an anhydrous organic solvent providing (1R,3S,5S)-1-acetoxy-3-hydroxy-5-(tert-butyldimethylsilanoxy)-cyclohexane I (R = α-OSiMe2CMe3, R1 = α-OAc, R2 = α-OH) in >99% ee and quant. yield was described.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 24 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:678967 HCAPLUS
DOCUMENT NUMBER: 121:278967
TITLE: Large scale preparation of chiral building blocks for the P3 site of renin inhibitors
AUTHOR(S): Doswald, Stephan; Estermann, Heinrich; Kupfer, Ernst; Stadler, Heinz; Walther, Willi; Weisbrod, Thomas; **Wirz, Beat; Wostl, Wolfgang**
CORPORATE SOURCE: Dep. Microbiol., F. Hoffmann-La Roche Ltd., Basel, 4002, Switz.
SOURCE: Bioorganic & Medicinal Chemistry (1994), 2(6), 403-10
CODEN: BMECEP; ISSN: 0968-0896
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Racemic Et 2-benzyl-3-(tert-butylsulfonyl)propionate (1) and racemic Et 2-ethyl-3-[[1-methyl-1-((morpholin-4-yl)carbonyl)ethyl]sulfonyl]propionate (3) were enantioselectively hydrolyzed by subtilisin Carlsberg generating the resp. (S)-acids used as building blocks for renin inhibitors. The esters were readily converted as emulsions at elevated temperature, in a suspended form or a two-phase-liquid system. The enzyme maintained its excellent selectivity and a good activity also at high initial substrate concns. (up to 50% weight/weight). The enzymic reaction and work-up were optimized and scaled up. Emulsion problems during work-up encountered with these highly concentrated mixts. were solved by application of a disk separator for phase separation

L26 ANSWER 25 OF 25 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:424763 HCAPLUS
DOCUMENT NUMBER: 117:24763
TITLE: Process for the preparation of optically pure (S)-α((tert-butylsulfonyl)methyl)hydro cinnamic

acid

INVENTOR(S): **Wirz, Beat; Wostl, Wolfgang**
PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Switz.
SOURCE: Eur. Pat. Appl., 6 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 475255	A2	19920318	EP 1991-114879	19910904
EP 475255	A3	19930414		
R: AT, BE, CH, DE, DK, FR, GB, IT, LI, NL				
JP 04248993	A2	19920904	JP 1991-254159	19910906
US 5223432	A	19930629	US 1991-756027	19910906
PRIORITY APPLN. INFO.:			CH 1990-2956 A	19900912

AB (S)-α((Tert-butylsulfonyl)methyl)hydro cinnamic acid (I) is manufactured from the corresponding racemic C1-C4 ester by stereospecific hydrolysis with a proteinase. The hydrolysis takes place in an emulsion of the substrate, a cosolvent, and water. (RS)-α[(Tert-butylsufonyl)methyl] hydrocinnamic acid Et ester 79 g in DMSO 105 g was mixed with water 6.2 L at 30° and brought to pH 7.5. α-Chymotrypsin 1.05 g was added and the pH held constant by addition of Ca(OH)2. After 19.5 h I 35 g (48.3% yield, 96.6% of theor.) with an ee >98% was recovered.

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